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The Colver Lectures in Brown University
1917

Medical Research and Human Welfare

By

William Williams Keen

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1861

1917

WILLIAM WILLIAMS KEEN

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Brown University. The Colver Lectures, 1917

MEDICAL RESEARCH AND HUMAN WELFARE

A Record of Personal Experiences and Observations during a Professional Life of Fifty-Seven Years

BY

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"It is desired that, so far as possible, for these lectures only subjects of particular importance and lecturers eminent in scholarship or of other marked qualifications shall be chosen. It is desired that the lectures shall be distinctive and valuable contributions to human knowledge, known for their quality rather than their number. Income, or portions of income, not used for lectures may be used for the publication of any of the lectures deemed desirable to be so published."

Charles Kendrick Colver (1821–1896) was a graduate of Brown University of the class of 1842. The necrologist of the University wrote of him: "He was distinguished for his broad and accurate scholarship, his unswerving personal integrity, championship of truth and obedience to God in his daily life. He was severely simple and unworldly in character."

The lectures already published in this series are: —

1916

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Fig. 4, Diphtheria Bacilli; Fig. 5, Typhoid Bacilli; Fig. 6, Tetanus Bacilli.

Figs. 1, 3, 4, 5, and 6 reproduced by the courtesy of W. B. Saunders Company from Dr. A. C. Abbott's *Hygiene of Transmissible Diseases.*

CHART I 76

Monthly Distribution of Calls for Malaria at Crossett, Ark., 1915 and 1916.

Reproduced by the courtesy of Mr. Wickliffe Rose of the Rockefeller International Health Commission.

CHART II 97

Mortality from Diphtheria in Fifteen American Cities before and after Antitoxin Treatment.

By the courtesy of the Prudential Insurance Company.

CHART III 99

Mortality from Diphtheria in Twenty Countries of the World before and after Antitoxin Treatment.

By the courtesy of the Prudential Insurance Company.

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PLATE II 104

Fig. 1, Different Phases of Development of the Malaria Parasite (Plasmodium).

After Thayer and Hewetson. From Dr. A. C. Abbott's *Hygiene of Transmissible Diseases.*

Fig. 2, Typhoid Fly Tracks.

By the courtesy of Prof. W. M. L. Coplin, Jefferson Medical College.

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From "Nitrogen-gathering Plants," by Karl F. Kellerman in *Yearbook of the Department of Agriculture for 1910.*

Fig. 2, Nitrogen-fixing Nodules of Alder.

From "Nitrogen-gathering Plants," by Kellerman.

Fig. 3, Fossil Bacteria from Montana.

By the courtesy of Prof. Charles D. Walcott.

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MEDICAL RESEARCH AND HUMAN WELFARE

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MEDICAL RESEARCH AND HUMAN WELFARE

A Record of Personal Experiences and Observations During a Professional Life of Fifty-seven Years

IN 1855, a young fellow of eighteen, without even a single acquaintance in Providence, I came to Brown, drawn by that intellectual magnet — Francis Wayland. At the Commencement Dinner I heard an old fellow of the class of 1805 respond for his class of half a century before. I looked at him askance and said to myself, "You old rascal, you ought to have been underground long ago and have left the earth to us young chaps!" But a long procession of the years has shamed me of my hasty judgment, for next June I shall celebrate my fifty-eighth academic birthday! I humbly ask of him a posthumous pardon.

How little I even dreamed that the most gilded future would bring me any such honor as falls to my lot to-day to address the University. This has done more than evoke my

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gratitude. It has caused me to review these more than six decennia. It has made me appreciate more than ever the extraordinary age through which I have lived, and the wonderful help that my Brunonian education has ever been to me in aiding humanity in some small measure towards health and happiness.

These reflections led me naturally to choose as my subject — "Medical Research and Human Welfare: A Record of Personal Experiences and Observations during a Professional Life of Fifty-seven Years."

HUMAN WELFARE

What are the factors that promote Human Welfare?

First, and by far the most important, is Good Health. Without that, one is crippled. Having it, one can achieve the rest, such as food, clothing, shelter, the other prime needs of the body, and for the mind, education, mental development, travel, books, pictures, and all the varied factors which collectively we call "Civilization." To them are to be added as far as possible the negative assets of life, such as freedom from sorrow and grief caused by

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death, especially the premature death of those dear to us.

To aid us in achieving those blessings and free us from those sorrows Medical Research is our best friend. The human mind — especially the medical mind — is never content with things as they are. We are ever seeking to decrease our ignorance and increase our knowledge; to make things better, to devise new means for health and happiness.

When the first man asked, "Why am I sick?" "How did I become sick?" "By what means can I get well?" Medical Research was born. For twenty-five centuries these questions as to health have been constantly and insistently asked and the medical profession has been trying to answer them.

For many centuries we had only clinical observation; that is, pain and the physical surface phenomena of the body of the patient — fever, eruption, swelling, wounds, fractures, and other accidents. Then in the sixteenth century the experimental method began slowly to arise.

By the *first* method we had to observe for years and in many patients, Nature's vagaries in different diseases and her different phe-

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nomena even in the same disease, after her haphazard method.

By the *second* method, in a short time the same observer, having the now known causes of human and animals' disease at his beck and call, induces in animals certain diseases under conditions chosen at will, varies these conditions one at a time, notes the differing results of each change, not only by his five senses, formerly his only allies, but by many instruments of precision wholly unknown fifty years ago and many of which even now cannot possibly be used on man. He can also verify his inferences not only by observing external phenomena, but by post-mortem examinations in animals of every internal organ at varying periods in the progress of the disease and so learn the "natural history" of the disease, the phenomena of its various stages, and the relative values of various remedies or operations.

This method is not only valuable in acute and fatal diseases, but may be even more so in protracted diseases when death from the original disease only reveals to us the end results, and not the early changes and later stages of the malady; while in non-fatal diseases, death

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gives us the results of the intercurrent fatal malady which obscure those of the original disease.

It is too often overlooked that for century after century Nature has been pitilessly performing her crude and cruel experiments and killing millions of human beings every year. She has inflicted untold suffering without any merciful anesthetic and with only occasional inadequate and passing relief by our narcotics. In place of these millions of human beings an infinitesimally smaller number of animals have suffered far less and far less acutely in research and have yielded extraordinary and most beneficent results as I shall show.

For seventy years past anesthetics, in practically all save a few cases in which an anesthetic would defeat the object of the experiment, have been used. Not only are anesthetics desirable from humane motives (and the whole world gladly credits my profession with abundant charity and humanity), but it is self-evident that delicate, modern, technical operations require the absolutely complete relaxation of anesthesia, to say nothing of the possible accidents to the operators themselves from struggling animals. Besides this, as I shall show,

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the knowledge derived from such researches, undertaken primarily for the benefit of humans, has been and will be shared by countless animals year after year.

Moreover, these researches have gradually enlarged our horizon so that now we recognize the "solidarity" of all living things.

That mysterious something, that wonderful reality which we call "Life," attains its highest and most complex development in the intellectual leaders of human thought and action. Life also reaches down to the lowest monad and the lowest plants which simply exist and reproduce their kind.

As we go down the series, the processes by which life is maintained become more and more simple; organs which perform precisely similar function in man, animal, or fish, such as the liver and the stomach, the heart and the lungs, are modified and at last may even disappear. Yet "Life," in its simplest activities of growth and reproduction, still is there.

The lower and simpler forms of life possess fewer and fewer weapons for either defense or escape, but preserve their species by the enormous numbers of their offspring to counterbalance wholesale destruction by their natural

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enemies. They also have the faculty of enormously rapid growth, not only in number, but in weight.

Fish provide huge numbers of eggs, as in our familiar shad roe, and the lowest forms of life multiply with an almost incredible rapidity.

The cholera bacillus divides into two, then four, eight, sixteen, and so on every twenty minutes, so that in seven hours, if given room enough and food enough, one bacillus would have produced four millions of descendants and in ten hours over two hundred millions. Each of these descendants possesses the same fecundity as its parent. What the number would be in a week or a month staggers one's wildest imagination.

The rate of growth of the silkworm in weight is equally astonishing. In the first thirty days after being hatched from the egg it increases in weight fifteen thousand times, or five hundred times its original weight every day. We can get a more impressive idea of what this means by comparing it with a human baby. Were the same rule to hold, a baby weighing seven pounds at birth would weigh thirty-five hundred pounds the very next day, and when a month old would weigh one hundred and five

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thousand pounds, or over fifty "short tons," which, however, could hardly be called "short weight." If you will pardon the abominable but expressive *argot* of the street, that would be "some baby." But we may be somewhat consoled by remembering that both mother and nurse would be of corresponding elephantine bulk — made to "fit the job" as the exponents of efficiency would say.

But this is a gross, unimaginative way of looking at such a phenomenon. When we analyze it seriously, what a wonder-world we enter upon. How these little worms must feed, feed, feed! Think of the abounding life of each microscopic cell. Every one has to multiply itself five hundred times in every twenty-four hours. Yet all goes on in an orderly manner according to the law of its being, but with incredible swiftness, day after day. The only wonder is that in such speed there should not be errors and mistakes by the thousand. Yet Mother Nature breeds true to her well-chosen model. And what superb work such a lowly, little worm does, for, presto! and the yellow cocoon becomes the resplendent silk and the glossy satin.

Animals closely resemble man not only in their structure and functions, but also in their

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maladies. Their diseases are often identical with human diseases and are caused by the same bacteria; e.g., tuberculosis, tetanus, anthrax, etc. What is true of the animal world applies with modification even in the vegetable world. Plants carry on a modified respiration and circulation, they assimilate food, their wounds are healed, their diseases, even cancer itself, are analogous to the diseases of man and animals, they are susceptible to the same poisons, they live, they grow, they reproduce their kind, and they die. These are all manifestations of that still, mysterious force which we call "Life." The physiology of animals and plants and the pathology of their diseases throw light on the problems of Human Physiology, Pathology, Health, Life, and Death. The man who, like Theobald Smith, devotes himself to the study of disease in many lower animals, has even a richer field to cultivate and may even have a broader vision than the man who limits himself to the diseases of man alone.

The latter half of the nineteenth century has been the period of the most marvelous activity in research in every branch of science, astronomy, physics, chemistry, etc., and not less in medicine and surgery. This progress has been

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made possible by the extensive use of the experimental method more than by any other means. Through all of this period I have lived and I have been able to avail myself of its beneficent discoveries for the welfare of mankind. I speak, therefore, of the things that I know and can vouch for personally, so far, at least, as surgery is concerned, and I have reliable evidence of the truth in other departments of medicine.

I took part in the old horribly fatal surgery of the Civil War and have borne a part in the struggle with infection and death until, thanks to Pasteur and Lister, we have emerged from a septic Purgatory into an aseptic Paradise. Only those who have lived through the transition period can fully appreciate the joy of deliverance from Death who formerly claimed, as his right, from five or ten to over ninety of our patients in every one hundred.

Much of this work has been done in quiet, thoughtful, thorough, ingenious researches in laboratories. After repeated careful tests upon animals, the results have been applied to the amelioration of human and animal diseases and the saving of human and animal life, as we shall see further on.

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It is a spectacular feat to rush into a burning building and at the peril of limb and life to emerge, singed and bleeding, with a precious child in one's arms, rescued from a frightful death. It is lauded by the entire community and rightly so. But to work quietly in the laboratory, surrounded by deadly germs, and to discover the antitoxin of diphtheria, a remedy which will rescue not one child, but thousands upon thousands of children year after year, — is not this a feat deserving a greater reward than that accorded to physical bravery? Too often such a modest laborer in the Master's vineyard is forgotten or never even known. But even then he has his reward, hidden it may be in his own bosom and known and recognized by his Maker — a greater joy than gold or jewels can yield.

In my early professional life, before such researches had been carried on, and the cause or the means of their prevention had been discovered, one single case of yellow fever, cholera, or plague in New York Harbor created terror in the whole city or even the whole nation, paralyzed commerce, and caused a wholesale exodus and widespread, most annoying quarantine. Now such a case scarcely wins a head-

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line on the first page of the morning papers, so complete and so justified is the confidence of the community in the ability of scientific medicine to cope with and to conquer the disease. Quarantine is no longer what its name declares — a detention of forty days. In fact it rarely is necessary, and when necessary is short and shorn of the horrors of a century ago. Even smallpox no longer sends everybody to the railroad, the steamship, and the auto, but sends them straight to the doctor, who quickly gives them the protection of a simple vaccination.

I bring you, therefore, a message of joy and good cheer, of wonderful achievement in every department of medicine and wonderful contributions to Human Welfare.

A NEW TYPE OF SURGEON

Experimental research has bred a new type of doctor and especially a new type of surgeon. Among the earlier pioneers were Harvey (1578–1657), Haller and John Hunter, both nearly contemporaries with Washington. But with the advent of Pasteur and Lister there opened the vast and virgin field of illimitable fertility

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in the new science of Bacteriology. Later, Fritsch and Hitzig, Ferrier and Horsley, whose recent death in Mesopotamia was a world-wide calamity, and others in Europe; Senn, Halsted, Cushing, Crile, and others in America have been the modern happy leaders

The older clinical surgeons observed shrewdly the phenomena of various diseases and injuries in the living, and the final phenomena in the dead, assembled in statistics the results of differing methods of treatment, including varied operative procedures, or of abstention from operation, and drew their final conclusions as to which method promised the best results.

The new type of surgeons, relatively few in number but potent in influence, hungering and thirsting for broader and more complete knowledge, restrict their actual surgical work so as to carry on researches in bacteriology, physiology, physiological chemistry, and physiological physics, and even as Carrel has recently done in what might be called "mathematical surgery," with its mysterious equations. Carrel can now predict to a day when a wound will be completely healed with almost the accuracy of an astronomer in predicting an eclipse.

The new surgeon pursues his studies in the

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laboratory as well as at the bedside and in the operating-room. He employs the second, the experimental, method of research as I have just described it. He tries new ways of operating or devises entirely new operations, which often require him to invent wholly new instruments.

When he has discovered any improved method or new operation and fully tested it in animals, then and only then does he venture to apply it systematically both to animals and to man. Thus, by intensive study and in a brief time have been introduced wholly new methods and multitudes of new and life-saving operations for the lessening of misery and restoration to health. The new surgery of the last forty years, with which many of you are reasonably familiar, has been the abounding harvest of these devoted Servants of Humanity.

Were I a physician, an obstetrician, a physiologist, an ophthalmologist, or other such specialist, I could make a similar showing. Indeed, before I end these lectures I shall have poached upon the preserves of a number of these my colleagues in our laborious but victorious campaign against Disease and Death.

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ANESTHESIA

It is almost superfluous for me to call your attention to one of the greatest boons ever conferred on suffering humanity — the abolition of the horrible pain attending surgical operations. This has done far more than merely abolish such pains. It has made possible prolonged and delicately difficult operations which require the absolute immobility of the patient. Imagine an abdominal section, such as is now common, with removal of a portion of the intestine followed by uniting the two open ends so carefully and so securely that no fatal leakage of a single drop shall occur. Such an operation, by reason of extensive adhesions or from other causes, may easily require an hour. Sometimes such an operation may require one and a half, or, though rarely, even two, hours. Could flesh and blood lie quietly, still as a statue, while such an operation was being done?

But beside the drugs for general anesthesia, Medical Research within the last thirty years has discovered means by which local anesthesia can be attained; that is to say, the part to be operated on is made entirely insensible to pain while the patient himself remains entirely con-

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scious. Nearly everybody has an innate aversion to loss of consciousness *per se*. This is wholly apart from fear. Various methods, by means of freezing, or the subcutaneous injection of certain drugs, such as cocain, novocain, eucain, etc., are employed. Besides their subcutaneous use these same drugs can be injected into the sheath of the spinal cord by lumbar puncture, thus making all the body below the waist insensible to pain. It is not within the scope of these lectures to assess the relative values and the dangers of these various methods, but only to point out how the marvelous resources of science have been mobilized for the welfare and comfort of mankind and of animals. Happy, indeed, are not only the surgeons, but also those engaged in experimental research, that investigations, such as Claude Bernard, Magendie, and others were obliged to carry on when anesthetics were unknown, and far more difficult and delicate operations than they even dreamed of, can now be done, and are done, painlessly.

The first public use of ether was at the Massachusetts General Hospital on October 16, 1846. Chloroform was first used on November 17, 1847. About 1867 the use of nitrous oxid came into common use in dentistry, and during the

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last ten to fifteen years has been largely used in surgery. All of these events have taken place during my own lifetime. Ether and chloroform were introduced during my boyhood; nitrous oxid and all methods of local and spinal anesthesia have been introduced during my professional lifetime. When I have heard my old master in surgery, the elder Gross, and other surgeons of his generation, tell of the way in which patients were bound hand and foot and held in the tight grip of four strong orderlies to secure a partial quietude, and of the almost frantic involuntary struggles of patients, and their screams of agony, in the pre-anesthetic days, I have thanked God that I was born too late to participate in such horrors. Then he was the best surgeon who could amputate a limb in five or ten seconds less than any other surgeon. The painstaking, accurate, artistic surgery, such as to-day is achieved by every good surgeon, was absolutely unthinkable even to the most dexterous surgeons in the first half of the nineteenth century. It had to be what, without casting reproach on our predecessors, one may call "slap-dash surgery" or none — and "slap-dash surgery" might easily be inaccurate surgery and do great harm.

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INSTRUMENTS OF PRECISION

Among the most important means by which Medical Research is promoted are instruments of precision. When I studied medicine, a few, in fact a *very* few, doctors possessed a microscope. Strange to say, the medical colleges themselves had none. Only those private students who were so fortunate as to have the most enlightened preceptors ever saw a microscope, much less had the chance to use one. I doubt if there were half a dozen thermometers and hypodermic syringes in the whole Army of the Potomac in the Civil War. A number of years passed before self-registering thermometers were made. The first short clinical thermometer I ever saw was brought to me from London by Weir Mitchell in 1876. The first book in medical thermometry was published by Wünderlich in 1869, four years after the Civil War closed. Imagine the plight of the mother of a family to-day without a thermometer!

Now, for experimental researches, there are electric thermometers by which one can make continuous observations in a hospital and record them at stations a mile away from the patient and the instrument. Mosso has de-

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vised an apparatus on which the patient lies, so delicately balanced that if he is spoken to, or a door is closed with a slight jar, even during his sleep, the brain is roused to activity — more blood is swiftly supplied to the brain, the head becomes heavier, and that end of the apparatus falls.

How and why, you ask, does this blood leave other parts of the body and go to the head? In man and animals, in close proximity to the jugular vein in the neck, is the sympathetic nerve — a slender, nervous cord, the use of which nobody knew. Just before the Civil War Claude Bernard cut this cord, "just to see what would happen." He found that the pupil of the eye on the same side contracted to a pin-point, the blood vessels of the ear of a cat or a rabbit dilated and the ear was much redder and hotter. This simple experiment opened the door to a vast store of knowledge. The sympathetic nerve is the means by which automatic changes are effected all over the body: changes which we cannot initiate and cannot arrest — changes which are essential to well being. This nerve controls the size of the pupil so that, on going out into bright sunlight, in a few moments it protects the eye from injury by contracting

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the pupil. On going into a darkened room it dilates the pupil so that enough light enters the eye for you to see.

This little nerve spreads out over every blood vessel all over the body, enlarges its diameter if blood is needed in any organ and lessens their caliber when the need has passed. When you eat a meal the stomach becomes redder than the most inflamed eye you ever saw. All its blood vessels are dilated to their maximum to enable the glands of the stomach to secrete enough gastric juice for digestion. When this is accomplished the blood vessels narrow and are scarcely visible. When you blush for shame or grow pale with fear, this slender, nervous cord has produced a dilatation or a contraction of the blood vessels of your face and neck, according to your emotion.

When you think, you need more blood in your brain. You do not, indeed you cannot, order it to go there and you do not have to keep up ordering it there. This is done for you automatically. Hence, even in your sleep, as we have seen, a voice, the jar of a closing door, may not even waken you, but your slender, sympathetic nerve never goes to sleep. It is ever on the alert to help you.

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When you are wounded the same obedient nerve automatically dilates the blood vessels, carrying the extra blood needed for repair, and the area around the wound is reddened and is hotter than the unwounded part. What a wonderfully beneficent mechanism this is — how useful — how indispensable!

And we knew nothing of all this astonishing action, so important in health and disease, in physiology, pathology, surgery, every department of medicine, until Bernard cut this little cord in the neck, to see what would happen!

If I only had the time I could tell you other equally interesting, in fact fascinating, stories of many discoveries in the physiology of digestion, of respiration, in the physiological chemistry of the blood and of the normal secretions, and in pathology or the changes brought about by disease. Our knowledge of all these subjects, instead of being the shrewd but uncertain guesses of close observers, has become exact and positive knowledge upon which we found not only our diagnosis, but our treatment. It is quite safe to say that in practically all diseases, save perhaps cancer, the death-rate is steadily and often rapidly lessening as a result of such scientific research. And we doctors who live

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by sickness and accident are the foremost in these researches and rejoice with joy unspeakable at every advance in the conquest of Disease and Death!

Many of my hearers are now familiar with the blood-pressure apparatus which in the last few years has won its place in diagnosis. Whole books are devoted to this one subject. In animals we can ascertain this pressure far more accurately than in man, for we connect the apparatus directly with the blood current in an artery or a vein. The pulse-beats and its curves are minutely analyzed by complicated instruments and recorded on smoked paper on a slowly revolving drum.

When, by reason of shock and loss of blood, the blood pressure during an operation falls so low as to be dangerous, we now can make a transfusion of blood. In certain diseases, as you all know from the daily papers, transfusion is also frequently resorted to. What you do not know is the long series of experimental researches on animals made by many surgeons, which has converted, what was so dangerous an operation that it had been abandoned, into a safe one. Now, thanks especially to the researches of that genius, Carrel, transfusion has

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become so safe that it is used even in cases of newborn babies who are bleeding to death, and are changed as by a miracle from dying babies into thriving and healthy babies.

The color of the blood is sometimes a very important element in deciding for or against an operation, or for or against giving an anesthetic. It can easily be determined by an instrument to measure the color of the blood. Its freezing point, the time necessary for it to clot, its bacteriology, and its chemistry all require constant research and are all constantly increasing in value.

But the instrumental study of the heart has progressed further than even the most vivid imagination could portray. By the X-rays we can see its size and witness its beating — a marvelous automatic act, the continuance of which dominates our existence from even before birth down to the last moment of life. Very recent improvements in the instruments now enable us to obtain X-ray pictures showing the action of each auricle and each ventricle separately.

All muscular action — note this fact — all muscular action generates slight currents of electricity. Therefore, the muscular contraction of the walls of these four cavities of the

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heart generate slight currents of electricity. Such a current, slight as it is, is sufficient to actuate another marvelously delicate instrument, the electro-cardiograph. By this we can record on a revolving drum the phases of movement of each of these four cavities.

The anatomists have discovered, at a point where the superior vena cava empties all the blood of the head, neck, and arms into the right auricle, a special network of muscles and nerves which Thomas Lewis, of London, has called the "pacemaker" of the heart, for the contractions of the heart are started by it. His, the German anatomist, some years ago discovered a similar small bundle of muscular and nervous fibers in the furrow between the auricles and ventricles which regulates the contractions of the ventricles. The auricles and ventricles, to use a rough but very simple simile, do not contract all four at once, as we would suppose, but in a rhythmical succession like the four feet of a horse. The "pacemaker" starts and the "bundle of His" regulates the successive rhythmical contractions of these four cavities. If the passage of stimuli, starting from these two points or foci, is interfered with, a certain number of impulses may be blocked and, for exam-

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ple, only one in two may get through. If the impulses are entirely blocked, the auricles and ventricles beat wildly and entirely independently of each other. These interferences are, therefore, called respectively "partial" and "complete heart block." By the electro-cardiograph we can study minutely every phase of such movements down to what occurs in the fiftieth part of a second. A diagnosis which it is absolutely impossible to make by touch and ear is positively and accurately observed by such a wonderful instrument of precision. It gives the very earliest warning of danger, long before our clumsy natural senses can find out that anything is wrong.

By the X-ray, as you know, we can now discover foreign bodies in the windpipe and lungs, in the esophagus, stomach, and intestines, stones in the gall bladder, kidneys, ureter, and urinary bladder; can see an artery whose walls have become hardened by arterio-sclerosis, can see foreign bodies and tumors in the brain, and can see even the convolutions of the brain, fractures, dislocations, tumors, and abscesses in bones, unsuspected abscesses at the roots of the teeth, tuberculous cavities in the lungs, cancer of the stomach, etc. By mixing bismuth with

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the food (bismuth is impervious to X-rays and so casts a shadow) we can follow the food from the stomach through the intestines. By this method Cannon, of Harvard, has shown the physical effect of fear and other emotions in arresting the digestive processes.

In 1891 Quincke, of Kiel, first introduced "lumbar puncture." A long needle attached to a hypodermic syringe is inserted within the sheath of the spinal cord, but below the cord itself, in the small of the back or "lumbar" regions and some of the fluid which bathes the cord and the brain is obtained. The pressure of this cerebro-spinal fluid is important and can be estimated, and the presence or absence of any foreign substance, such as blood, pus, certain bacteria, etc., can be determined by the microscope. An unsuspected fracture of the base of the skull may declare itself by such blood. No diagnosis of cerebro-spinal meningitis is accepted at present as scientifically proved except by lumbar puncture. Without this a large percentage of mistakes occur.

All of you are familiar with at least a few of the ingenious "scopes" by which we can look into various cavities of the body. Helmholtz, of Berlin, that wonderful genius, first showed

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the way by devising the "ophthalmoscope" in 1851. In 1858 Czermak, of Prague, devised the "laryngoscope." This was so new when I entered the Jefferson Medical College in 1860 that to my almost incredulous inquiry "whether it was really possible, as Green, of St. Louis, asserted, actually to see the vocal chords in a living patient," my preceptor, later the distinguished Professor J. M. DaCosta, replied rather hesitatingly that he "thought" it was!

Now we look not only into the interior of the eye and the larynx, but down into the bronchi, into the esophagus, and even inspect the inside of the stomach, the bladder, and every other hollow organ accessible from the exterior.

To explain how great has been the advance in knowledge of function and in diagnosis and treatment by reason of the positive information obtained by these various instruments of precision, and how much our patients have benefited by this new knowledge would take me too far afield, but in a general way I may say that to them is due practically, I should say seventy-five per cent of our present knowledge of the diseases of the organs susceptible to this method of examination. Without these ingenious instruments physiologists, physi-

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cians, and the surgeons and specialists would be as utterly helpless as if in our community life our railroads and steamships, our telegraphs and telephones were suddenly abolished.

Turning now to individual medical researches which have made great contributions to Human Welfare, I must content myself with the story of only a few of the most notable, for to recite the whole long catalogue would expand these lectures far beyond reasonable limits for even your friendly indulgence. My "Bill of Particulars" to which I now turn must therefore be a restricted one.

Two great achievements in modern medicine before my professional studies began in 1860, were vaccination in 1796 by Edward Jenner, and anesthesia, first introduced publicly to the profession on October 16, 1846, when I was over nine years old, by Morton and Warren, at the Massachusetts General Hospital.

BACTERIOLOGY

The third great achievement was the discovery of the causal relation of bacteria to many diseases. Thus arose a new science — "Bac-

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teriology" — the most important discovery *ever* made in pathology. It would scarcely be an exaggeration to say that Bacteriology is the most important discovery *ever* made in *any* department of medicine, for upon its revelations hang most of our modern surgery, and a very large part of the advances in modern medicine and in modern obstetrics. Bacteriology is also the foundation of a very large part of modern sanitary science and of much of our agricultural success.

While bacteria had been named and known for many years, they had not been classified and coördinated into a science until about thirty years ago. The earliest use of the word "Bacteriology" dates only from 1884. With the rise and development of Bacteriology must always be associated three illustrious names: Pasteur, Lister, and Koch; especially the first two.

PASTEUR'S AND LISTER'S ACHIEVEMENTS— SPONTANEOUS GENERATION

I was in Paris as a student in 1865 when the scientific world was stirred to its depths by the great contest over spontaneous generation. One of my teachers was a son of Pouchet, Pas-

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teur's principal opponent. Pouchet published experiment after experiment in which it seemed impossible at first sight to explain how the living organisms arose in his sterile flasks except by spontaneous generation; but with marvelous genius Pasteur always found some unguarded portal of entrance. For instance, Pasteur not only sterilized the contents of his flasks and then sealed them, while boiling, but high up in the Alps, held each flask above his head when he broke the neck of the flask with sterile forceps. Even the direction of the wind was evoked in his behalf. If the wind blew over the opened flask first and then over his body, no infection followed. If he turned around so that the wind swept past his body first and then over the opened flasks, it carried germs from his person and his clothing, and infection followed. Such minute precautions are now the A B C of Bacteriology — then they were wholly new and even derided as unnecessarily meticulous.

Up to the time of Pasteur's experiments putrefaction was believed to result from the action of the oxygen of the air on the putrescible substance. Pasteur, and later Lister, by as simple an experiment as that of Columbus

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and the egg, proved the falsity of this belief. Lister filled four glass flasks one third full of urine, a most easily and quickly putrescible fluid. He then drew out the necks of the flasks into fine tubes less than one twelfth of an inch in diameter. The neck of one flask was left vertical and open to the air. The necks of the other three were bent downwards at various angles but were left open. Each flask was then boiled. This sterilized the inside of the flask as well as the urine. All four were kept together in the laboratory. The air with its oxygen, as the night grew colder, was slowly drawn into all four flasks and slowly expelled as the air grew warmer in the morning. In a short time the flask with a straight neck underwent putrefaction. The three with necks bent downward, but freely open to the air, remained perfectly free from putrefaction for *four years*. The explanation is clear. The germs in the air drawn into the flask with the vertical straight neck fell directly into the fluid and caused its speedy putrefaction. In the air drawn into the flasks with bent necks, the germs being slightly heavier than air, settled on the sides of the neck of the flask and never reached the fluid. The oxygen entered all flasks alike.

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The final result of many experiments and prolonged controversy was that the impossibility of spontaneous generation was absolutely established. *Omne vivum e vivo* was proved to be true. Only life can produce life.

Lister, and especially Pasteur, discovered, proved, and compelled the acceptance of the germ theory as applied to putrefaction and opened the way to the means of its prevention. The same principles apply to the causation of infection in wounds and of many diseases in animals and man and their prevention or cure.

It is a fascinating story. The "Life of Pasteur," by his son-in-law, Vallery Radot, is the most inspiring scientific biography I know. Its title in the earlier editions wins us by its wit and modesty and is really untranslatable from the spirituelle French into our clumsier though virile English: "Louis Pasteur. La Vie d'un Savant par un Ignorant."

Pasteur was born in 1822 and died in 1895 at the age of seventy-three. About the middle of the nineteenth century, when he was in the early thirties, we "did not know much more of the actual causes of the great scourges of the race, the plagues, the fevers, and the pestilences, than did the Greeks," as Osler has well

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said. He then continues: "Here comes in Pasteur's great work. Before him Egyptian darkness; with his advent a light that brightens more and more as the years give us ever fuller knowledge."

PASTEUR'S LIFE AND WORK

Pasteur began his life-work in crystallography and by his exact observation explained why two kinds of tartaric acid turned polarized light the one to the right and the other to the left. All through his life he longed to return to his "dear crystals." But God had mapped out a far more beneficent career for this Apostle of Science.

He studied the repair of wounds in crystals. Breaking off a piece from an octahedral crystal he replaced the wounded crystal in the mother liquor. After a time the wound was healed and the crystal was again perfect.

Next he placed one of the salts of racemic acid — a compound (as he had already discovered) composed of the right and left polarizing tartaric acids — in the ordinary conditions for fermentation. Only the dextro-tartaric — the right polarizing — acid fermented.

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His explanation was that the *living ferments* attacked and fed upon only this one form of the acid. *Per contra,* if he cultivated a little *penicillium glaucum* — a lowly fungus — on the surface of ashes with one of the other forms of tartaric acid, there was produced only the left polarizing tartaric acid. These were phenomena of *life of a physiological order.* Thus was he led by his crystals to study the changes produced by the lowest forms of living beings in physiological and finally in pathological conditions in animals and man. Thus Bacteriology, after multiplied labors and experiments, was born.

The year 1855 found him in the University of Lille, a "mere chemist," as his adversaries called him. He knew nothing of medicine, and never became an M.D. Yet we doctors all pay him enduring homage as one of the greatest of our guild — truly an "Honorary Member."

Lille was a town of great breweries and Pasteur's services were soon enlisted in the study of the diseases of beer, which led him again to study fermentation in all its varied forms in beer, wines, vinegar, alcohol, sour milk, and rancid butter. He carried over the exact methods of the chemist, but along with it the imagi-

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nation of the seer, into this new realm of Biology. He disproved the then prevalent belief of Berzelius and Liebig that fermentation was due to a so-called "catalytic" influence of a certain substance — acting simply by its presence. I learned this catalytic theory at Brown and had to unlearn it. Pasteur proved conclusively that fermentation was due in all cases to a *living substance*, such as the yeast plant, or the "mother" of vinegar, or similar vegetable organisms in all fermentations.

These studies produced in his mind the idea that diseases of humans like diseases in beer, in wine, in milk, in butter, might be due to microscopic germs floating in the atmosphere, an idea which was to fructify into great discoveries, destined in the hands of Lister to revolutionize medicine, surgery, and obstetrics, and to prove of untold value to man and animals. The key to Pasteur's methods is found in his dictum, "In experimental science it is always a mistake not to doubt, when facts do not compel you to affirm."

Then, in Paris, followed the contest over spontaneous generation, to which I have already alluded.

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THE SILKWORM

Next, Pasteur's genius was sought in an effort to save the great silk industry of France. This industry was threatened with extinction by an extraordinary and inexplicable mortality of the silkworms. He had "never even touched a silkworm." But he was equal to the task. After a long and laborious search, with many puzzling apparent contradictions, he finally discovered that the silkworms had been destroyed by *two* diseases. One of these, named "pébrine," was caused by peculiar germs called "corpuscles" and the other, called "flachery," by an infective micro-organism.

Then the problem was solved. The eggs of all the silkworms in whose bodies the "corpuscles" of "pébrine" were discovered were destroyed and only the eggs of healthy worms were used for breeding. Ordinary precautions against infection prevented "flachery." The latter was not hereditary, the former was. A national calamity was averted.

In 1868, when only forty-six years of age, Pasteur's labors and even his life were threatened with complete collapse. His entire left side

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was suddenly paralyzed. Gradually, however, he recovered and, wonderful to relate, his very best work was done during the next twenty years. While he never entirely regained the use of the paralyzed side and always had a bodily limp, yet, fortunately, his active mind never limped, but strode onward conquering and to conquer.

ANTHRAX

Another of his great achievements which again blessed his always idolized country was soon accomplished — the conquest of anthrax. This is a very ancient disease. Is is believed to have been the murrain of the Egyptian plagues. It is a very fatal disease in men as well as in cattle. In Italy from 1890 to 1902 the annual toll of human lives was 2100, and in Russia from 1904 to 1909 it cost as many as 16,000 human lives a year. Fortunately with us cases of the disease are rare.

Anthrax was then devastating the sheep and cattle of France and costing also many human lives. Animals grazing over certain fields suddenly fell ill and quickly died. Pasteur proved that even from buried carcasses of animals

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dead of anthrax, the worms brought the anthrax germs up to the surface and that animals browsing over such a field became infected and died. Men who handle even their hides, long after the animals have been killed, fall victims to the disease, so that we know it in this country chiefly as "wool-sorters' disease," from the source of the infection. The germ may live as long as twelve years and still be deadly. It has spread all over Europe and a number of outbreaks have occurred in America.

I have only time to describe two of Pasteur's experiments, one upon hens, the other on sheep and cattle, ending in his triumphant vindication.

In 1850 Davaine first noted, but only as a curious fact, that in the blood of animals dead of anthrax little rods or bacteria existed. (Plate I, fig. 1.) In 1863, after reading a paper on fermentation by Pasteur, Davaine had even asked himself whether possibly these little motionless rods might not act as ferments — like yeast — and be the cause of the disease.

In 1877 Pasteur began his researches. He cultivated the bacteria from the blood of animals dead of anthrax. By inoculating a sterile fluid with a drop of this first culture he obtained

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FIG. 4. Diphtheria Bacilli as they appear with three different methods of staining

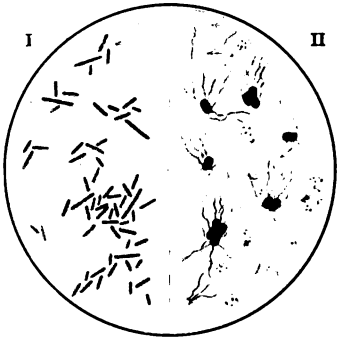

FIG. 5. Typhoid Bacilli
I. Stained by ordinary methods
II. Stained by Loffler's method, showing the processes (*flagella*)

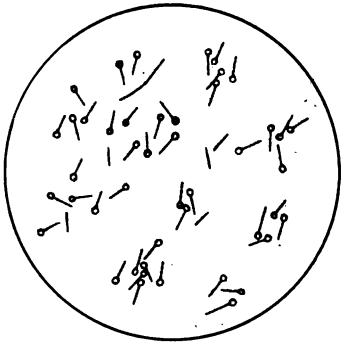

FIG. 6. Tetanus Bacilli

PLATE I

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FIG. 1. Anthrax Bacilli
(The dark rods)

FIG. 2. Hookworm
Natural Size

FIG. 3. Tubercle Bacilli
(The delicate beaded rods)

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a second, from this a third, and so on up to one hundred generations, and found that the one hundredth culture would kill as certainly as an injection of the blood itself.

Among other animals hens had been inoculated with anthrax germs, but they always survived. Pasteur became interested in this curious exception and finally found the reason for their exemption. The normal temperature of the hen is several degrees above that of sheep and cattle. This higher temperature he believed prevented the growth of the anthrax bacilli. To test this important point in the life history of the bacilli, he inoculated hens and then lowered their temperature by cold baths. This so reduced the temperature of the hens that the anthrax bacilli could multiply and the hens died the next day. A few degrees of temperature more or less held the balance between life and death.

One ingenious experiment clinched his argument. A hen was inoculated with anthrax and held in a cold bath until it was evidently very ill with anthrax. Then the hen was taken out of the bath, dried, wrapped up in cotton, and recovered entirely. Her temperature fell in the bath so that the anthrax bacteria grew and

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made her ill, but when her temperature rose after removal from the bath the bacteria were killed and she recovered.

It is startling for us humans, with all our physical and mental superiority, to find that we too are at the mercy of such almost infinitesimal lowly plants which break through and steal our health and often our very lives. Happily, however, Pasteur showed the way to escape from this danger. I can give you a personal instance of the speed and violence of the invasion of such bacteria. Many years ago, at a *post-mortem*, I pricked my thumb with a needle very slightly. In fact I hardly knew that I had pricked myself. In eight hours I began to feel chilly, in twenty hours my temperature was 105°. I barely escaped with my life.

Note what a temperature of 105° means. It means that my one hundred and fifty pounds of flesh and blood had the temperature raised from 97.5° F. to 105° F. or 7.5°; and not only was it raised to that height, but it would have been kept there or would have gone even higher until death supervened. But modern surgery came quickly to my aid. Under ether the thumb was widely opened and thoroughly disinfected and my life was saved.

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Pasteur's last triumphant experiment as to anthrax was dramatic. He had discovered by many experiments that the anthrax bacteria could be cultivated at 42° or 43° C., but in a weakened form; i.e., they never develop "spores," or, as I may call them, "seeds." At 45° C. the bacteria themselves could no longer be cultivated. You see now the value of his experiments on hens! He was now ready for the *experimentum crucis*.

He proposed by this attenuated virus to vaccinate twenty-five healthy sheep against anthrax. Then later to inoculate these twenty-five vaccinated sheep and twenty-five other healthy but unvaccinated sheep with a virulent virus of anthrax. He predicted that by a certain day every one of the twenty-five vaccinated sheep would escape death and every one of the twenty-five unprotected sheep would die. It was, indeed, a decisive test. One of his opponents said: "He *must* succeed. . . . Let M. Pasteur not forget that the Tarpeian Rock is near the Capitol."

On May 5, 1882, at the Pouilly le Fort farm near Melun, a large crowd of people, farmers, doctors, veterinary surgeons, and others, assembled at this memorable rendezvous to see

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Pasteur's vindication or his humiliation. The first twenty-five sheep were then inoculated with the protective vaccine. On May 17 a second protective inoculation was given to the same twenty-five sheep. On May 31 the final inoculation, this being an anthrax virus of full strength, was given to all the fifty sheep, twenty-five protected and twenty-five unprotected. By June 5 he declared that all the unprotected twenty-five would be dead and the twenty-five protected would all be alive.

On June 2, three days earlier than his predicted date, when Pasteur arrived, he was loudly acclaimed the victor, for there already lay the dead carcasses of twenty-two of the unprotected sheep and the other three were dying, while all the twenty-five vaccinated sheep were in good health!

All France rightly rang with his praises. The method has been adopted everywhere, and by this vicarious sacrifice of a few sheep countless flocks and herds have been rescued from the suffering and death to which they were doomed by Nature's cruel experiments. Their owners have been saved from enormous pecuniary loss and millions of human beings have been provided with so much more wool, more hides, and

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more meat as a sequel to that memorable day. Our enterprising and most useful Agricultural Department has discovered a serum even more potent as an antidote than even Pasteur's. To insure and standardize its strength it is always tested first on rabbits.

PUERPERAL FEVER

But a still greater triumph marked these same years — the conquest of puerperal or childbed fever. This fever is the most humiliating incident in the history of medicine. In these antiseptic days the ravages of this fell disease are almost unknown. But a quarter of a century after the ink had dried on my own medical diploma, the obstetrician — who should usher in a new life — was too often a sower of the seeds of death.

In the Pennsylvania Hospital from 1803 to 1833 every eighteenth mother left her newborn baby motherless. In 1872 Lusk, of New York, reported an epidemic in which one mother out of every *five* died! In my own early professional life I knew of case after case proving fatal, and in some epidemics the *accoucheur* for a long interval had to relinquish practice entirely, for

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Death always peered over his shoulder and slew every fifth, fourth, third, even every second, mother. A mortality as high as fifty-seven mothers out of every hundred has been recorded! Its mystery, like the pestilence that walketh in darkness and the destruction that wasteth at noonday, spread fear among doctors and expectant mothers.

Oliver Wendell Holmes in 1843 declared that the doctors and nurses themselves carried the dreaded infection, but how or why no one knew. In 1861 Semmelweiss, in Vienna, preached the gospel of cleanliness anew, but was derided and even ostracized. Pasteur, however, compelled a hearing throughout the world: what is better, he was the victor.

In 1879, — less than forty years ago, — in a debate at the Paris Academy of Medicine, the leaders were at odds as to the cause of this fever and were totally ignorant of any means for preventing it. Suddenly interrupting an eloquent colleague discussing the various possible causes, Pasteur declared that puerperal fever was of bacterial origin, and was carried by the doctors and nurses. His colleague retorted that he feared that this strange microbe would never be found. Thereupon Pasteur at once stepped

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to the blackboard, and drawing what we know as the streptococcus, said, "Voici la figure!" (There it is!) And there it was, indeed!

And what has been the result of the researches by which Pasteur demonstrated the cause of childbed fever and how to abolish it? Every wife and every husband should know these facts and treasure Pasteur's memory in their hearts. Instead of every eighteenth, every fifth, or more than every second mother lost to her husband, her children, and the community, puerperal fever now slays only one mother in three hundred to even so low a rate as one mother in twelve hundred and fifty! Verily Pasteur was one of God's best gifts to Humanity.

CHICKEN CHOLERA

Chicken cholera was a serious malady in France until after Pasteur's researches in 1882. Healthy fowls would suddenly sicken and die within a day or two, again from a mysterious disease without apparent cause. Once more Pasteur waved his wand and light shone in the darkness. He had discovered the germ, and by inoculating healthy hens, was searching for

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a vaccine against it similar to the anthrax vaccine. One day by accident he injected a culture from an *old flask* standing on a shelf in the laboratory and forgotten for a few weeks. The hens thus accidentally inoculated with this old virus sickened, recovered, and when tested with strong virus, withstood it and remained well. The vaccine was found. To mediocrity the happy accident that it was an old culture would have been merely a curious fact to be recorded. To genius it was a fertile idea to be explained and developed by experiment. We shall see this in a moment when considering hydrophobia.

SWINE PLAGUE

Next swine plague was investigated. "Send me one thousand francs," he wrote. "I have but three hundred francs left. . . . Pigs are expensive and we are killing a great many." "Killing a great many?" True. But how many thousands and hundreds of thousands has he saved by the sacrifice of the few score which he called "many"? It is the old story of the fifty sheep at Pouilly le Fort farm — a vicarious sacrifice sanctioned both by science and humanity.

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HYDROPHOBIA

I have only time to record one other service by Pasteur; but this is his notable victory over that horrible disease called rabies in animals and hydrophobia in man. Pasteur's mind had been irresistibly drawn to this malady by its mysterious nature and by his previous studies. In 1881 he began his researches. His investigations showed him that, whatever its nature (and this germ, mark you, like that of yellow fever, has not even now been discovered), this virus centered in the spinal cord, especially in its upper end. After the bite of the rabid animal there was always a long period before the disease would develop — a period of weeks and even months of anxiety and suspense. Finally Pasteur tried the experiment of injecting some of the upper end of the spinal cord of a dog dead of rabies directly into the brain of a rabbit, from that rabbit to another, and to another, until, instead of months of uncertain waiting, he was able to induce the disease in fourteen days and later in seven days, thus greatly facilitating its study. Remembering his remarkable experience in the weakening of the virus of chicken cholera and of anthrax by time,

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he now placed the spinal cords of a number of dogs suspended by a thread in sterile sealed jars. In the bottom of the jars was some caustic potash to absorb the moisture and facilitate the drying. By many experiments on various animals he at last found that a cord which had hung in such a jar for two weeks could be injected into the brain of animals and that rabies did *not* follow. Then he tested on the same dog material from a cord after thirteen days of drying, later from a cord which had been drying for twelve days, and so on until the experimental dog was so fully protected that even the strongest fresh virus had no effect.

Victory again was his. But only a victory over the disease in animals. Dare he use it in humans? "My hand will tremble," said he, "when I go on to mankind." He shrank almost in terror from injecting into a human being the virus of rabies. What if perchance it should give the patient an attack for which he would be responsible?

At last Nature forced his hand. On July 6, 1885, the mother of an Alsatian boy of nine, named Joseph Meister, brought him to Pasteur. *Two* days earlier he had been attacked by a rabid dog and received fourteen wounds.

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Anxious to help the child, yet fearful of harming him, after consulting with some friends, Pasteur began the treatment with fear and trembling. First he used a cord dried for fourteen days, then one dried for thirteen days, then for twelve days, and so on. But what anxious days and nights he spent! He could neither work nor sleep. He was beset even in his dreams by visions of the child in the grasp of the demon of hydrophobia. On July 16, still with fear and trembling, he injected finally material from a cord which had been dried for only one day. Some of the same cord injected into rabbits was followed by rabies in the rabbits. But the boy remained well. Gradually his fears subsided as time went on and the boy still remained perfectly well. His final triumph was achieved.

In the following October another boy was inoculated *six* days after being bitten. He too recovered. From thenceforward the remedy was used more and more freely with lessening fears and growing hopes.

Before Pasteur, of one hundred persons bitten by rabid and supposed rabid animals, dogs, wolves, foxes, etc., about sixteen fell victims to hydrophobia. Of these sixteen *every one* died.

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There is not, I think, a single well-authenticated case of recovery after the disease has developed. The mortality of all those bitten is, therefore, about sixteen per cent — the mortality in actual cases of the disease is one hundred per cent. From 1885 to 1905 — twenty years — there were treated at the Pasteur Institute over twenty thousand persons, and the mortality for the last few years has been 0.32 per cent; that is to say, nearly fifty times less than in the days before Pasteur. In 1915 of six hundred and fifty-four persons bitten, instead of one hundred and five deaths, — the number which would have occurred before Pasteur, — there was only *one* death!

Naturally the patriotic fervor of the French quickly led to the establishment in Paris of an "Institut Pasteur," founded by popular subscription of over two and a half million francs. Among the names of the donors stands that of the little Alsatian boy, Joseph Meister, whose gift was the greatest of all those cast into the treasury. All over the world Pasteur Institutes have been established, and their record of success everywhere has been practically the same.

Muzzling of all dogs would banish hydro-

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phobia. How cruel we are to refuse to cause slight discomfort to dogs and thereby to sacrifice human lives.

No more devoted patriot than Pasteur existed. His efforts were always for France. "Nothing would have consoled me," said he of his vaccine against anthrax, "if this discovery had not been a French discovery."

His whole life is redolent with patriotism. When he was informed that a village in Algeria had been named after him, he wrote: "When a child of that village asks what was the origin of the name, I should like the schoolmaster to tell him simply that it is the name of a Frenchman who loved France very much and who by serving her has contributed to the good of humanity."

The same lofty patriotism has breathed a new life into the heart of France to-day. Lately, when the family and friends of a young recruit about to leave for the trenches assembled at a dinner in his honor, and some one proposed as a toast the health of the young man, his mother quickly rose and cried, "Non, non, — à la Victoire." We Americans should learn that same lesson. We may easily have need for it. [Since this was written we too have

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entered the war for Freedom and Humanity. May the same fervid patriotism be ours!]

Well might Huxley say that Pasteur's discoveries alone would suffice to cover the vast German war indemnity in 1870.

Think of the services of this "mere chemist." His first discoveries were in crystallography. He discovered the real cause of fermentation and then of putrefaction. He laid the ghost of spontaneous generation. He built the foundations of Bacteriology. He proved the germ theory of disease. He saved for his beloved France the several industries of beer, of wine, of vinegar, of silk, of cattle, of poultry, of swine. Better than any one or all of these he showed how to abolish childbed fever and hydrophobia among his fellow-men.

Fifteen victories and not one Waterloo! Where can we find a parallel?

Sir Humphry Davy, when asked what was his greatest discovery, instantly replied, "Michael Faraday." Had Pasteur been asked the same question he might well have replied, "Joseph Lister." The greatness of a nation is to be judged by the number of the great men it has produced. "Worship great men," said Pasteur to the students at the University of

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Edinburgh, all unconscious of the splendid egotism of his maxim. To-day in another university we gladly pay reverent homage to Pasteur and Lister, two of the world's greatest benefactors.

ANTISEPTIC AND ASEPTIC SURGERY

In his very first paper on "Antiseptic Surgery," in 1867, Lister proclaimed his large debt to Pasteur. Antiseptic surgery, as developed in its basic principles by Lister, is the greatest "revolution" in the entire history of surgery. I need only give brief consideration to its triumphs, however, since it has been the theme of many others besides myself, not only in the surgical press, but in many magazines both lay and scientific, and even in newspapers so that all intelligent persons have a fairly exact knowledge of its immense value. Its inevitable successor was aseptic surgery.

In fact it is a not uncommon lay criticism of some loitering surgeon who has not kept up with the progress of surgery, that he neglected this or that technic in the well-established ritual of antisepsis.

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MODERN SURGERY

I can give you only a faint idea of the blessings of modern surgery by a brief résumé of a few of its many blessings.

Wounds are either accidental, or, as in operations, intentional. If we can care for accidental wounds within the first twenty-four hours or less, we can almost certainly prevent infection by bacteria. This means that there will be little or no inflammation nor any discharge of pus. That means immediate and almost painless healing. Thus, compound fractures, in which the bone protrudes through the skin, instead of killing two out of every three patients, as in my early professional life, at present have a mortality from infection of only one in several hundreds if treated early.

If an ulcer of the stomach perforates and so allows the contents of the stomach to escape, this was formerly inevitably fatal, but now is not often fatal if treated early.

Appendicitis has almost no mortality if treated early. Early — if possible immediate — care by a competent surgeon, in all such accidents, is the surgical "slogan." In fact that is true of almost all surgery.

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In my own early experience practically every wound, intentional or accidental, became an infected wound. During the Civil War I cannot recall a single wound that was not infected, and many a time in summer I have seen them swarming with maggots — as large as chestnut worms — disgusting, but not especially dangerous guests. The mortality of wounds, and especially of gunshot wounds, was fearful. Blood-poisoning was frequent and its death-rate 97.4 per cent. Lockjaw often was seen and exacted a toll of over 89 per cent. Ordinary operations had a mortality of 15, 25 and 50 per cent or over. In consequence of the horrible pain in the days before anesthesia, and the terrible death-rate before antisepsis, no wonder that operations were as rare in those days as now they are frequent, for to-day Pain and Death are almost set at defiance.

If the wound is intentional, as in removal of a tumor or an amputation, we can almost always prevent infection, and if there is no extensive imperative operative mutilation recovery is almost certain. Gallstones are removed, parts of the intestines are excised and the two open ends of the bowel are reunited, thus re-establishing the continuity of the bowel, tu-

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mors of the liver are removed, stones in the kidney, or even one entire kidney, may be removed with wonderful success. Before the first human kidney was ever removed by Simon in 1870, by experimental removal of one kidney he established the fact that animals could survive with only one kidney. In 1887 I removed one kidney from a young woman on account of a gunshot wound. For two or three days it was doubtful whether the remaining kidney would be equal to the twofold load, then it quickly doubled its secretion, and she would have recovered had not another injury from the bullet, not discoverable at the operation, produced a fatal hemorrhage fourteen days later. The *post mortem* showed that the second kidney had increased twenty per cent in size during the fourteen days that she survived. When the necessity is laid upon her what can Mother Nature *not* do?

When nerves are cut or shattered by a knife or a bullet, or when a bad fracture tears a nerve, we sew the nerve ends together, and if, again, we can operate early, we can generally remedy the injury and practically without danger. Thus the not very uncommon birth-palsies of an arm, and the wrist-drop from frac-

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ture of the arm-bone around which winds the nerve, supplying the muscles which bend the hand backward, are remediable. In one case I deliberately cut out two inches of the arm-bone because the ends of the nerve were so far apart that they could not be sewed together. The cut ends of the shortened bone were then wired together, the nerve ends met and were united, the wound closed and speedy recovery took place. In a few weeks the patient had perfectly normal wrist and hand movements.

The mortality of amputations is now only ten to fifteen per cent, instead of fifty to sixty in every hundred, and only one patient in a hundred dies after an ovariotomy. We transplant portions of skin and pieces of bone as in an orchard we graft fruit trees.

The horrible wounds of the face and jaws in the present war, which at first sight seem hopeless, by transplanting parts of ribs or portions of the shin-bone, and then patching and eking out the flesh and skin, are transformed in a few weeks into faces which will pass muster as to usefulness and comfort, though, if you will pardon the phrase, they would not often win a prize in a beauty show.

The surgery of the head has been wholly

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transformed in the last thirty years. Abscesses are opened, tumors or portions of the brain are removed from patients who before 1885 were always all allowed to die. Tic douloureux, that demon of pain, can now almost always be exorcised.

The surgery of the chest has long lagged behind that of the rest of the body. When the chest is opened the corresponding lung collapses and the other lung may easily be unable to do double work. If both sides are opened, death quickly follows unless means are at hand for instant artificial respiration. But within the last few years we have learned by experiments on animals that a tube can be inserted into the windpipe and by a bellows we can carry on artificial respiration with ether-laden air until, when the operation is completed, the chest wall can be closed and normal respiration be reëstablished. By this method we can now reach the lungs, the heart, and all the other organs in the chest and operate upon them at will. Portions of the lungs can be removed, abscesses opened, coins and other foreign bodies which have been inhaled or swallowed, if they cannot be removed through the mouth or by operation in the neck, sometimes

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can be reached by this heroic and successful route.

"The road to the heart is only a little over an inch in length in a direct line," says Professor F. S. Lee, "but it has taken surgery nearly twenty-four hundred years to travel it." In 1897 Rehn, of Frankfort-am-Main, published the first successful case of sewing up a wound of the heart. The need for such an operation is most frequently a stab wound. The operation is a marvelous feat, for the sewing must be done while the heart lies in the surgeon's hand and keeps on beating. Now over three hundred cases have been reported and nearly one half of them have recovered.

Contrast this most imperfect list with what could be done in surgery when I graduated (1862). We then amputated limbs with a fearful mortality, removed a few external tumors, and buried a large percentage of our patients. One of the most common operations — for cancer of the breast — had a long and painful convalescence and a large mortality. Now it has a negligible death-rate and recovery follows in a week or two. Then we rarely operated for hernia and with little success. Now we cure practically all hernia cases and without any

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mortality. A few other operations were done — and the list comes to an end. In a large and active hospital there were only about three important operations in a month. To open the head, the chest, or the abdomen was then almost equivalent to a death-warrant. Now you can do almost anything — *provided you know how.*

All the operations I have mentioned, and many others, have been introduced during my professional life. Operations have now been made safe and, therefore, are frequent — ten, twenty, twenty-five a day in an active hospital. Thousands, who a half-century ago were doomed to suffering and death, are restored to health and joyful life chiefly because of the researches of Pasteur, Lister, and their many successors. Sanitation has helped much, but never overlook the fact that nearly all modern sanitation, apart from engineering proper, is based upon Bacteriology, the lusty daughter of Experimental Research.

SYPHILIS

I know of no more striking instance of the value of experimental research and of Bacteri-

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ology than the very recent and impressive discoveries in syphilis.

For four centuries this disease has ravaged the world. Tuberculosis and alcohol and syphilis may be called the greatest physical enemies of the human race. During all those four hundred years it had been studied clinically by many of the wisest and shrewdest surgeons. We had learned how to abate its evils to a considerable extent, but we knew not the cause nor any real cure. It never occurs naturally in animals. Many attempts had been made to inoculate them so as to study the disease experimentally, but always without success. Suddenly, in 1903, Metchnikoff, whose recent death is such a loss to science, succeeded in inoculating some higher apes. Since then we have learned how to inoculate other animals. Now mark the instant progress, the wonderful progress in our knowledge, directly due to animal experimentation.

Two years later, in 1905, Schaudinn and Hoffmann discovered the germ of the disease. The diagnosis of the disease could now be made with certainty, not only during its active existence, but years and years later when the diagnosis was generally inferential and uncertain.

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In 1910, seven years later, Ehrlich discovered a cure. His recent death is another calamity. In these *seven years* more was learned as to the cause and cure of this terrible scourge than in *four centuries* of observation. This cure is the result of the most phenomenal patience and perseverance in the whole history of research.

Ehrlich was led for certain reasons to use arsenical preparations. On inoculated animals he tested one preparation after another, but found this one too dangerous, that one ineffective, others impracticable for one reason or another. But his mental and his chemical resources never failed. The lengthening list of preparations tried and tossed aside grew to one hundred, two hundred, four hundred, and six hundred without a single entirely satisfactory result. Imagine what six hundred complicated tests mean. What a splendid optimism, what a robust faith, must have pushed him on and ever on! Finally, the six hundred and sixth experiment succeeded! Improvements have followed a widening experience. We have learned that it is not an infallible cure. But for the vast majority of cases it is the very best and most reliable means we have and rarely fails.

Think of the results to the whole human race!

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Think, above all, what it means to the multitude of innocent victims; and thank God that such wonderful power for good has been vouchsafed to man!

This discovery of the specific value of arsenic to kill the germ of syphilis without harming the patient is an instance of the specific action of a particular drug which I earnestly hope may foreshadow other discoveries of a similar character.

We have a second specific remedy in quinine which kills the germ of malaria — an animal parasite in this case — without harming the patient.

Mercury, when given in large doses, produces "salivation" with loss of the teeth — a harmful specific action. Still more remarkably localized is the well-known destructive action of phosphorus, from which so many workers in match factories suffered before the making of phosphorus matches was prohibited by law. Phosphorus not only selected the bony framework for its field of action, but limited its effects to one particular bone — the lower jaw.

At the Rockefeller Institute, Dr. Walter A. Jacobs and his co-workers are now engaged in promising researches in an endeavor to find

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chemical substances which will prove specifics to kill various bacteria without injury to the patient. If they discover any such remedies against the bacteria which cause infections such as abscesses, erysipelas, puerperal fever, etc., they will have opened a new era in medicine. Instead of external antiseptics to combat infection locally, these new internal synthetic antiseptics will attack the germs wherever they exist in the entire body.

Some former world-wide plagues may be considered here seriatim.

SMALLPOX

As I have limited myself principally to the researches during my professional lifetime, I shall only allude briefly to what has been done in smallpox since 1860. One of my own students, Dr. Victor G. Heiser, who was for a long time the efficient Director of Health in the Philippines, has performed one enormous experiment on human beings that deserves notice. He has vaccinated over eight million people between 1905 and 1915 without a single death! In India during the year 1914 to 1915, 9,462,901 people were vaccinated, again with-

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out a single death! When one remembers the uncleanly habits of the masses vaccinated, and that every vaccination is a small surgical wound, and unless properly protected is liable to infection with all its serious danger of blood-poisoning, these two series of vaccinations were marvelously successful.

Moreover, Heiser has told me the striking story of the results in over one million vaccinations in and around Manila. Before his vaccinations there were every year about six thousand deaths from smallpox. In the twelve months following the completion of his vaccinations in the same area, there was not one single death from smallpox! *Could any person with common sense ask for better evidence* of the protective value of vaccination?

By a curious coincidence another disastrous, unauthorized experiment was made in the Philippines which is a striking contrast to that of Dr. Heiser. On one of the small isolated islands, with a population of two thousand, an old woman, instead of protective vaccination, inoculated a number of persons with the smallpox pus from a human case. An epidemic of smallpox immediately broke out, resulting in one thousand cases, half the entire population,

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four hundred of whom died. As quickly as the facts were learned by Dr. Heiser, vaccinators were sent immediately to the island. Eight hundred of the remaining one thousand unvaccinated inhabitants were immediately vaccinated. There were no cases and no deaths from smallpox in these eight hundred who had been vaccinated. The other two hundred ignorant, superstitious people fled to the mountains and nothing is known as to their fate.

The epidemic of 1885 in Montreal teaches a similar lesson. A Pullman porter reached Montreal as his attack of smallpox was just beginning. That one case resulted in 3164 deaths and probably disfigured or blinded from ten thousand to twelve thousand persons, to say nothing of the expenses attendant on the illness of so many persons and the great pecuniary loss to the merchants of that city.

During the Civil War and later once in Philadelphia, I have passed through three epidemics of smallpox, and I do not hesitate to say that it is the most loathsome disease I know and its results in those who recover are the most repulsive and pitiful.

One objection against vaccination has been urged that tetanus is sometimes produced by

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an impure vaccine. This statement is entirely erroneous. Whenever tetanus has followed vaccination (as it may follow *any* wound), the United States Public Health Service has investigated the cases and "in no instance could it be shown that the disease was attributable to the virus."

CHOLERA

I need do no more than refer to this pestilence, for that we have got the whip-hand of it is a matter of common knowledge. But *how* have we done so? Largely sanitation — a clean water-supply and a vigilant prompt segregation of every case. But the imperative need of a clean water-supply had been disclosed and enforced by the discovery of the microbe of cholera and that this microbe was the water-borne means of spreading the epidemic. Medical Research has also taught us how to cope with such an epidemic.

The causes of cholera, plague, malaria, and tuberculosis have all been discovered during my lifetime. We have cut down their mortality enormously and our future success will be even greater.

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One great obstacle to the total elimination of diseases, such as cholera and some other diseases, is that Medical Research has shown that there are "cholera-carriers," carriers of typhoid, of cerebro-spinal meningitis, etc. "Carriers" are persons who have had an attack of cholera, typhoid, etc., have recovered, and yet the bacteria of the disease still linger in the nose, mouth, or intestines for months and even years.

In other cases the germs of the disease seem to have invaded their bodies without producing any illness whatever, or at least any recognizable illness, and have become permanent inhabitants in their economy. In one German camp, during the present war, after an outbreak of cholera, five such carriers were found among six hundred men. In Calcutta, in 1915, bacteriological examination suddenly disclosed a large number of cholera germs in the water-supply. The whole community seemed to be threatened with an impending outbreak. Immediate examination showed that the Hindu who gathered the samples of water for bacteriolgical examination was a cholera-carrier. His elimination from the service eliminated at once the bacilli from the water-supply.

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Typhoid-fever-"carriers" have been followed by serious outbreaks of typhoid in every family in which they have been employed. In the present war such carriers of cerebro-spinal meningitis have been a serious menace to the men in the trenches.

How to rid such carriers of their infective microbes is an extremely difficult problem and as yet not fully solved. It is also a sociological and legal question of importance. The community, of course, must be protected, yet to hold such an innocent carrier as a prisoner is abhorrent to our idea of justice. Research in time will find the means to free the carrier from the infection and free him from detention.

BUBONIC PLAGUE

In Bombay, in 1902, the bubonic plague was killing over one hundred natives every day, yet I stayed in the city for over a week and had no fear. The "cantonment" or European quarter was wholly free from the disease. Why this marked difference?

Medical Research — I wish I might tell you the interesting story in detail, but I have not the time — Medical Research has shown that

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the rat-flea carries the infection from the rat to man. Hence the plain lesson. What Carthage was to Cato the rat is to the modern sanitarian. *Delendus est.* In the European quarter of Bombay all the rats were destroyed; in the native quarter the destruction of animal life was taboo, for might not a human soul be enshrined there in one of its many transmigrations?

You may recall what Rupert Blue, then a subordinate of the Public Health Service, now its able Surgeon-General, did in San Francisco. Besides looking after the patients themselves, he trapped and poisoned every rat, and rat-proofed their possible places of refuge. For eight years there has not been a case of plague in San Francisco. The last infected rat was found seven years ago.

In the New Orleans outbreak of 1915 nearly five hundred thousand rats were caught; two hundred and sixty-five infected rats were found in nearly three hundred thousand which were examined, and the epidemic was arrested.

The germ of the plague, the "bacillus pestis," was discovered in 1894 by Yersin and Kitasato and our immunity from epidemics is due solely to Bacteriology. Haffkine discovered, also by Bacteriology, a vaccine which reduced the case

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mortality from 60 per cent to 24 per cent. Yersin, of the Pasteur Institute, has apparently improved upon this.

YELLOW FEVER

Another veritable romance of medicine of surpassing interest is the discovery of the means of the total prevention of yellow fever.

The cause of smallpox and the cause of yellow fever have so far eluded the most intense and unintermittent search by many astute and persevering men. But that they will be found I have not the slightest doubt. It is only a question of time. But in both of these terrible diseases we have found the means for their prevention and, if medical advice were universally followed, for their total eradication.

In 1847 Mott, of Alabama, advanced the theory that insects may be carriers of disease, and in 1876 Dowell, of Galveston, called attention to the similarity of the natural laws governing the gnat and the mosquito and yellow fever, but without result. In 1881 Carlos Finlay, a graduate of the Jefferson Medical College of Philadelphia, declared that yellow fever was

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transmitted from man to man by the *stegomeia* mosquito, but his words fell on deaf ears. In 1898 the careful observations of Henry R. Carter, of the Marine Hospital Service (now the Public Health Service), gave important support to the mosquito theory. Finally the American Commission — how proud I am that they were my fellow-countrymen! — in 1900 positively proved that Finlay was right.

The problem was most complex. There are about four hundred varieties of mosquitoes, yet the Commission were able to identify the two which carried, one, the yellow-fever germ, the other the malaria germ. They discovered that only the female is the biter. They found that the female mosquito must bite a yellow-fever patient during the first three days of the fever, and that then it requires twelve days for the germ — still unknown — to develop in the body of the mosquito. There was still much incredulity; many still believed that yellow fever was carried by clothing, bedding, etc., — the so-called "fomites." To disprove this mode of infection the doctors slept for many nights in the soiled clothing in which yellow-fever patients had just died, they tried every repulsive method by inoculation, even to swallowing the

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black vomit, but all in vain. Not one of them contracted the fever.

Then came the supreme test. No animal can be inoculated with yellow fever. The only possibility of the test was in human beings who would allow themselves to be bitten by mosquitoes known to be infected. Who were the very first to offer themselves? The doctors of the Commission themselves. Agramonte barely escaped with his life; Lazear lost his young, promising life for the sake of Humanity — a sacrifice as noble as any young warrior hero in a forlorn hope.

To-day we owe our immunity from yellow fever to these heroes of medicine.

The last case of yellow fever contracted on the Isthmus of Panama was in 1905—*nearly twelve years ago!* Never again can there be a great epidemic of yellow fever in the United States. Those of you who have read Weir Mitchell's "Red City" will appreciate what a wonderful triumph this is for Medical Research.

The Yellow-Fever Commission of the Rockefeller Foundation has just returned from a careful investigation of the various foci of infection in South America. Guayaquil is the principal source of infection, with one or two minor possi-

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ble foci. Yellow fever is reported to exist in Mexico and on the west coast of Africa. It behooves us immediately to bestir ourselves, for otherwise the opening of the Panama Canal — a veritable Pandora's box — may easily result in serious epidemics of yellow fever in countries in which it is as yet unknown.

A systematic campaign against the mosquito and for the adoption of the sanitary measures found to be so successful on the Isthmus may enable us to banish yellow fever from the whole world.

MALARIA

This is a foe almost as deadly and far more widely spread than yellow fever. Living in the temperate zone we do not appreciate how deadly it is in tropical, and even semi-tropical, countries. In 1908, in India, malaria in a malignant form burst upon the province of the Punjab and killed nearly *three hundred thousand* persons in two months. The decadence of Greece has been attributed to the introduction of infected *anopheles* mosquitoes by immigrants in the fifth century B.C.

After a most careful investigation the Inter-

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national Health Commission of the Rockefeller Foundation describes malaria as "a disease which, taking the world as a whole, is probably the heaviest handicap on the welfare and economic efficiency of the human race."

The value of protection from the malarial mosquito is well shown by the recent experience of the United States man-of-war Des Moines in the harbor of Tampico. When the ship cleared for action all the screens had to be removed. Immediately, out of a crew of 293, 219 fell ill of malaria.

"No mosquitoes, no yellow fever"

"No mosquitoes, no malaria"

are axioms of tropical sanitation.

The International Health Commission, in cooperation with the United States Public Health Service, is making three remarkable experiments to discover the best means of dealing with this tremendous problem. In each case small malarious communities were selected so that the cases could easily be identified. In each town they are testing one, and only one, method. The first is solely by abolishing the breeding-places and therefore the number of mosquitoes without expensive drainage; the second is by only screening the houses; and the third by

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using quinine as a preventive without any other measures.

The result of the first method is very striking, and, as Mr. Wickliffe Rose, the Director of the Health Commission, writes me, is "no longer an experiment, but a very satisfactory demonstration." In a town with a population of 2029 persons the number of cases of malaria month by month during 1915 began in January with 40, by June reached 125, by August 350, and by October 600 cases. By December it had rapidly fallen to 100 cases. In January, 1916, there were 35 cases, the maximum of only 120 cases by May and by December had fallen to four cases. The total number of cases in 1915 was 2500. The simple, inexpensive measures adopted cut this number to 743 in 1916, and in succeeding years will undoubtedly show even better results. (See Chart I.)

While not eradicated, malaria in that town is no longer a serious menace. Screening and quinine in addition will certainly much further reduce the number of cases of malaria in the future and even beget a hope of the ultimate extinction of this vast plague.

A French army surgeon, Laveran, in Algeria in 1880, discovered the cause of malaria, an

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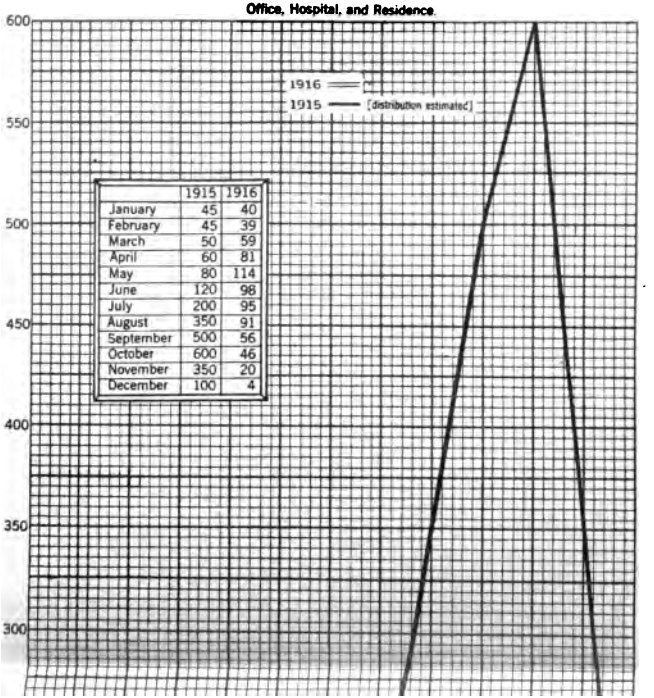
MONTHLY DISTRIBUTION OF CALLS FOR MALARIA AT CROSSETT. ARK.

Pop. 2029

Office, Hospital, and Residence.



	1915	1916
January	45	40
February	45	39
March	50	59
April	60	81
May	80	114
June	120	98
July	200	95
August	350	91
September	500	56
October	600	46
November	350	20
December	100	4

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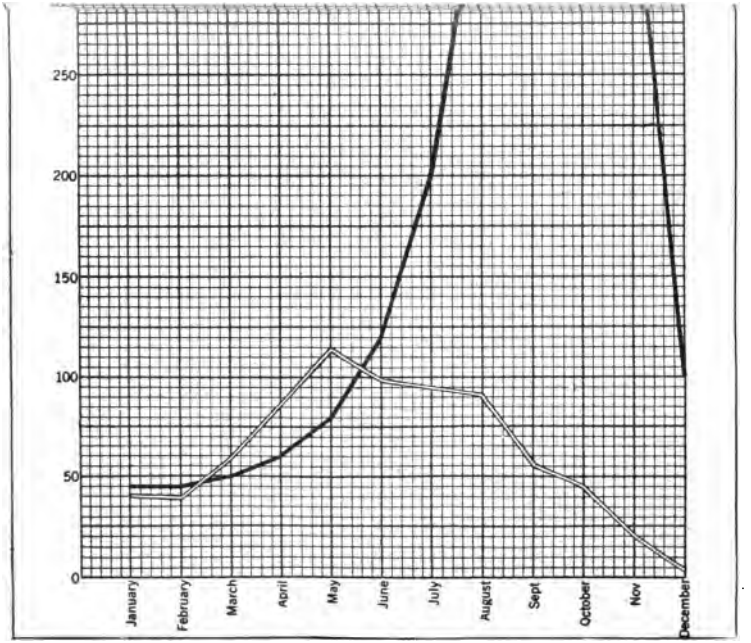

CHART I

For explanation see text. Reproduced by the courtesy of Mr. Wickliffe Rose of the Rockefeller International Health Commission.

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animal parasite, which, like the unknown germ of yellow fever, has two phases of life, one in the mosquito, the other in the patient. (Plate II, Fig. 1.) No longer is "a touch of malaria" allowable as a cloak for our ignorance of the cause of any illness. Now, if the parasite is found in your red blood corpuscles you have malaria; if they are not found, you have not.

Ross in malaria-ridden Secunderabad, after experimenting in vain on a long series of mosquitoes, bred for the purpose in his laboratory, on August 15, 1897, had just eight left. Six gave no results; the seventh seemed to point the way; in the eighth and last he reached his goal. "These two observations solved the malaria problem." The parasites were found, not as had been supposed in the stomach, but in the salivary glands of the mosquito. The exact route of infection of this disease which annually slays its millions of human beings was now revealed. "Never in our dreams," said Ross, "had we imagined so wonderful a tale as this." A single mosquito can infect several persons, and in view of the number of these pests it is easily seen how whole communities may be attacked. These experiments again were made upon unselfish doctors.

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It is a strange fact that the malarial and the yellow-fever mosquitoes, and the goats infected with the germs of Malta fever (*vide infra*), seem to be in no way deleteriously affected by the germs they harbor.

What has been the result on the Isthmus from the work of General Gorgas? Before this, the greatest experiment in sanitation ever tried in the world, among 45,000 employes, — more than an army corps, — the mortality while the French were digging the Canal was 240 per 1000. In 1913, among 56,000, an increase of 25 per cent in numbers, the mortality was 8.35 per cent per 1000, almost *one thirtieth* of the former rate.

General Funston had 24,000 men at Vera Cruz in 1914. Although Vera Cruz was an ill-kept tropical city in which smallpox and typhoid fever, and an epidemic of cerebro-spinal meningitis were rife, yet not a single case of any of these diseases was reported in our troops.

Our huge and splendidly successful experiment on the Isthmus has shown that the white man can live and work in the tropics, and yet maintain his health. This achievement is of far greater importance as to the Welfare

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of the Human Race than even the splendid engineering success of constructing the Canal itself.

The work of Dr. Heiser and his staff in the Philippines has been quite on a par as to usefulness with that done on the Isthmus by General Gorgas and his collaborators. It is not as widely known as it ought to be, and it is, therefore, with pleasure as a friend and pride as one of his teachers that I call attention to it in a very few words. The number of deaths has been lowered by about 75,000 per annum. The death-rate in Manila has been reduced from 43 per 1000 to 23 per 1000, not a bad showing for a large city in the tropics. Smallpox, as already indicated, has been almost conquered. Bubonic plague has been extirpated and cholera controlled. Heiser has put in operation a city sanitary code that is said to be more complete than that in use in any other large city in the world.

In several countries his organization of the Health Department in the Philippines has served as a model on which they have built — a recent compliment being a similar action by the State of Massachusetts.

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HOOKWORM

The name describes the parasite. (Plate I, Fig. 2.) It lives in the human intestines. It has been known for eighty years, but only in 1898 did Loos discover the portal of entry. It penetrates the skin of the hands, feet, etc., and in time reaches the intestine. In the newspapers it is called the "bug of laziness." But this is a serious misnomer. The victims of the malady are not "lazy." Their development, both physical and mental, has been retarded. They are indolent from incapacity, not from unwillingness. Dr. E. K. Strong, of the Rockefeller Foundation, has shown that even completely cured children gained mentally only sixty per cent as much as normal children; i.e., that they had less than two thirds of the mental capacity of normal children. Moreover, the longer they had suffered from the disease the greater was their mental loss and the more slowly did they progress toward the normal. If the disease had lasted a considerable time it was doubtful whether they ever could reach a normal mental development.

Physically its victims are relatively several pounds lighter in weight and it may be even

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some inches under the normal height for children of the same age. The moment they were cured immediate and rapid increase in weight was observed.

The story of the hookworm campaign by the Rockefeller Foundation is a story of wonderful interest and will in time bear wonderful fruit. In 1915 this campaign covered ten of our Southern States and eighteen foreign countries.

Hookworm disease extends over a belt nearly four thousand miles wide, girdling the whole earth from 36° north latitude to 30° south latitude. It includes the United States south of San Francisco and Richmond, all of Central America and the West Indies, South America as far south as Buenos Aires and Santiago di Chile, all of Africa save Cape Colony, all of Asia Minor, Persia, India, Southern China, Korea, and Japan, the Philippines, all of Australia and most of the Pacific groups of islands. This belt includes more than half of all the inhabitants of the entire globe.

You see, therefore, the hugeness of the problem of its extermination, but I firmly believe that the attempt will succeed. Careful microscopic examinations of the excreta of almost a million and a half of people all over the world

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showed the minimum infection of over twenty-seven persons out of every hundred, and the maximum in Ceylon, where on certain plantations only four persons out of every hundred were free. Recently in the East he even found some places where practically every person was infected.

The worm differs wholly from the familiar infectious bacteria. It does not multiply in the human intestine. Each individual worm expelled by purgatives has entered the body by penetrating the skin from without and then has literally "wormed" its way to the intestine. As many as six thousand have been expelled from a single patient.

Thymol and oil of chenopodium are efficient remedies. In Porto Rico three hundred thousand patients were cured and their efficiency at once increased by twenty to thirty per cent.

The way in which the disease is spread is not an agreeable study, but it is one that must be told plainly or the seriousness of the menace to ourselves in our Southern States and all over the world in the wide equatorial belt will not be appreciated.

Our smug satisfaction with our splendidly

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elaborate and costly sanitary plumbing receives a terrible jolt when we learn that in the twentieth century, in a highly civilized country as we profess to be, a detailed examination of 287,600 farmhouses in eleven of our Southern States disclosed the fact that 142,230 had no cesspools of any kind whatever. Of these 287,600 farmhouses only six tenths of one per cent! — i.e., 1726 — had satisfactory arrangements to prevent soil infection by the dejecta. The hookworms in this infected soil lay in wait for every barefoot person who walked over it.

The means of the entire extirpation of this disease are theoretically very simple and very certain: (1) Cure those now infected by the treatment mentioned; (2) make everybody wear shoes; and (3) compel the introduction of efficient cheap latrines of such a character as to prevent further soil infection.

All this is very simple on paper, but when you come to put it in practice it soon discloses itself as a problem not so much of legal compulsion as a huge problem of education of six to seven hundred million people of all degrees of civilization, the majority, perhaps, of low, often the very lowest, intelligence, speaking

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hundreds of different languages and under many rulers in the great equatorial "hookworm belt."

But that in time it will succeed, especially as country after country sees convincing proofs of the value of those measures, I have a firm belief.

I am proud that such beneficent, far-reaching plans have been laid in my own dear country and that more than one of my own students have had a hand in the work.

TUBERCULOSIS

Tuberculosis — the "Great White Plague," or "Captain of the Hosts of Death," as it has been truly and picturesquely called — in 1914 killed 96,000 persons in the "registration area" of the United States. As this covers only two thirds of our population it is a fair inference that in 1914 it destroyed 144,000 lives in the United States. What a huge loss of life; what a huge loss of effective power; what a huge expense to pay the bills incurred in their care and their burial; and finally, what a huge wave of suffering in its victims and of sorrow in their families and

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friends! And yet in 1914 its ravages had been greatly curtailed from what it was fifty years ago.

Not only have its ravages been curtailed, but the mental attitude of the public and of the patients themselves has been changed. When I started in medicine, once that a patient was pronounced "consumptive," all hope was gone, he was a doomed man, the only question was, "How short will his life be?" Moreover, his descendants were believed to be in the shadow of the same disease. In 1866 I taught my classes that tuberculosis was positively *contagious*, for Villemin a year earlier had discovered and proved this by injecting tuberculous tissue and sputum into rabbits. That was an immensely important discovery and occurred even before we knew the cause, for Bacteriology did not then exist. Sixteen years later, after Pasteur and Lister had established the truths of Bacteriology, came the momentous, the all-important, discovery of its cause. I well remember that Monday morning in 1882 when the editorial staff of the "Medical News" gathered to decide on the editorials for the next Saturday's issue. A cable had just been received announcing Koch's discovery of the

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tubercle bacillus. The late Roberts Bartholow wrote the editorial announcing the epochal discovery.

Our sanitary precautions are practically all based on that happy discovery. We learned then how and why the disease spreads. Coughing, laughing, sneezing, spitting by tuberculous patients, eject the tubercle bacilli into the air, on to the pavement or the floor or the clothing, there to dry, to become pulverized, and to be inhaled by the well. Hence the danger in the use of common utensils, such as drinking-cups. When it was proved that fresh air and sunlight were active enemies of the tubercle bacillus, the fresh-air cure, including sleeping out-of-doors instead of in closed rooms, became the vogue. Then we learned how to diagnose tuberculosis by the microscopic examination of the sputum or the excreta for tubercle bacilli far earlier than by its physical signs; i.e., by percussing and auscultating the chest. The microscope was the sentry which gave the alarm, and called at once for the mobilization of our sanitary and therapeutic forces to combat the invading bacillus. Then we learned that scrofula, that Pott's disease of the spine resulting in a hunch-

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back, that the so-called "cold abscess" which was so chronic and entirely free from heat, that many diseases of bones and joints, were all different forms of tuberculosis. Still later have come the "tuberculin" test by which we safeguard ourselves and especially our children from tuberculous milk, and several other technical tests by which we can detect tuberculosis even in its very beginning and in latent and otherwise undetectable stages.

Our errors were corrected, our treatment became simplified and scientific instead of empirical. Then the death-rate began to fall. In Boston, for example, in the twenty years before Koch's discovery (1882) the death-rate from "tuberculosis" was 420 per 100,000. In fact it was much higher than 420, for "tuberculosis" then included scarcely any cases except tuberculosis of the lungs. Twenty years later the death-rate had fallen to one half (210), and since then it has fallen to 180 per 100,000 and below. All over the world, where its Bacteriology and the consequent necessary sanitary measures are known and practiced, the death-rate has fallen nearly or quite to one half, and is steadily falling still lower.

If only we could completely control every

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case, tuberculosis could be extinguished in twenty years. The keystone of this Triumphal Arch of Progress is the discovery of the tubercle bacillus only thirty-five years ago. And what does this veritable little "beast" look like in the microscope? It has to be stained in order to see it well and then each bacillus looks much like one of the short colored threads in our bank-notes. It is as motionless as they — but it is a deadly enemy. (Plate I, Fig. 3.)

CANCER

There seems to be little doubt that cancer is growing in frequency as a cause of death and always with terrible suffering. It is, therefore, a pressing question.

No other enemy has been more persistently assaulted in the last twenty-five years — not even tuberculosis. It has been attacked by the clinician, the pathologist, the microscopist, the comparative pathologist, by all the resources of experimental research, by the X-rays and radium, by special Institutes and Endowments in Europe and America. We have stormed the outlying forts, but this grim Verdun of disease has not yet capitulated.

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For experimental research mice are chosen on account of their very short lives and ready susceptibility to infection. In a short time many generations can be bred and tested. For man, only three or four generations could be studied in an entire century, and meantime the student himself would have died with his work hardly more than begun. Moreover, our studies would be limited to the cases occurring naturally. No experimental work could be done on man.

I should add that these cancerous mice which I have often watched and held in my hand, even when bearing a cancer nearly as large as themselves, were as alert and lively as usual and showed not the slightest evidence of any pain or even discomfort.

In mice by appropriate matings we can now produce at will a race of descendants with a cancer rate as high as sixty to seventy per cent or one as low as nine per cent. The explanation is not easy. It may be that there is a disturbance in the normal balanced development of the multitude of differentiated cells of the various tissues arising from the unicellular ovum. In cancer this normal balance is lost. Instead of a development predetermined for

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each organ the cells of cancer run riot. Instead of performing a useful function as all normal cells do, the cancer cells grow without serving any useful purpose in the body. What factor produces this difference we do not yet know.

On the contrary, as is strongly suggested by the remarkable work in cancer in plants by Dr. Edwin F. Smith, of Washington (*vide infra*), it may be due to either an unknown, probably filterable, and, therefore, excessively small, almost undiscoverable bacterium or to an animal parasite.

The cancer problem is one not limited to man. It is a large problem of general biology for it attacks not only man, but the lower animals, birds, fishes, and even plants. Smith, as we shall see later, can produce what seems to be really cancer in plants at will by a hypodermic injection of his *bacterium tumefaciens*.

But mark my word — *the cancer problem will be solved by science*. That will be, indeed, a happy day for us surgeons when we have found the cause. We shall then be hot on the trail of the cure and that, too, without operation as we sincerely hope.

Meantime we know of only one real cure — the knife. Radium and X-rays and high fre-

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quency currents are useful in a small percentage of cases — but too often they delay the radical remedy till it is too late, and so, in fact, increase the mortality.

But remember that the knife is only dependable in the early, and if possible the *earliest* stages. If every man and especially every woman were to submit to the knife — now used without any practical danger to life — one per cent or less in skillful hands — the *moment that a lump was found*, the deaths from cancer would be only twenty-five per cent, or twenty per cent, or even less. Thirty years ago I would have told you that I had never cured a single case, but had only postponed the final event. The very few cases of permanent escape I believe were cases of mistaken diagnosis. Now, you see that this somber picture has been painted out, and hope has replaced despair. Some of my cases are still alive and well after ten, twenty, or even twenty-five years.

Remember, too, that persistent moles and warts, especially the dark-colored ones, are always a menace to life. Many of them, like the Lassen Volcano in California, long quiescent and seemingly innocent, suddenly burst into rapid growth, and then, even though ex-

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tirpated at once, are often fatal. They ought to be removed *before* they begin to grow.

Any lump, anywhere, which is not normal, with few exceptions demands immediate removal. It cannot be too strongly stated that in its early stages cancer is *always a local disease*, and in very many cases is permanently curable. In its later stages death is assured in a rapidly increasing percentage. Even though Medical Research has not yet found its cause, it has proved its curability, in the early stages.

DIPHTHERIA

I have a fierce hatred of diphtheria. When I was twelve it strangled to death a younger playmate brother, my parents' "Benjamin." When I was thirty it slew a sweet little niece and desolated another brother's home. It almost killed my dear friend Weir Mitchell. It robbed him of the wife of his youth and a daughter of his later life. For nearly thirty years during an active surgical life, I met it again and again, literally in a life-and-death struggle for the life of little children, and again and again it has defeated my best efforts to save them. I had the small comfort that at

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least they were not choked to death, but fell victims to the somewhat less cruel poison of the disease. No wonder that I hate it!

How often in those dark days have I stood, as it were, knife in hand, by the bedside of a gasping child, until at last the worn and sobbing parents could overcome their horror and permit me to try the last desperate surgical means of relief — a tracheotomy; i.e., making an opening in the wind pipe to prevent slow suffocation — but alas, so often fruitless. Now, thank God, it is many years since I have had to resort to a tracheotomy, for the blessed diphtheria antitoxin has practically abolished tracheotomy in diphtheria. Note these words "*has practically abolished tracheotomy in diphtheria.* Death still claims some victims, but its harvest is scanty and is steadily lessening, as I shall show.

In 1883 Klebs and, later, Loeffler discovered the germ of diphtheria. (Plate I, Fig. 4.) In 1890 Behring in Germany and Kitasato in Japan, by inoculating goats first with very small and then with gradually increasing doses of the toxin of diphtheria, as Pasteur had done in anthrax and hydrophobia, found that these animals could finally withstand the strongest

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doses, which would have been quickly fatal at the beginning. These animals had become immune, and, what is better still, the antitoxin thus developed in their blood, if injected into a healthy animal, such as a horse, made that animal immune by producing in its blood the antitoxin. When the blood serum from such an immune horse is injected into humans they are made immune, *not by the blood serum of the horse itself*, for only a small quantity is injected, but because this small quantity induces in the blood of the humans so inoculated the production of a new antitoxin of their own; i.e., *each patient is enabled to manufacture his own antitoxin.*

Not only is this antitoxin a prophylactic, i.e. preventive, but it is curative; and curative precisely in proportion to its *early* use, because the earlier it is used, the more quickly does the blood of the sick child produce its own defensive antitoxin.

To the surgeon it has brought untold relief as well as to the patient and family. Tracheotomy for diphtheria, as typified by my own personal experience, I repeat, has practically disappeared. Such frightful cases as were frequent before 1895 have ceased to be. No one,

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save an old surgeon like myself who has gone through many such harrowing, heart-breaking experiences, can appreciate the joy of our present deliverance. Could there be a better contribution to Human Welfare?

Nature never tired of her thousands of cruel experiments on children. The doctors did not experiment on children, but by quiet research in the laboratory, surrounded by a few rabbits and guinea pigs, worked out the whole antitoxin treatment. When certain of the results on animals, then they used it in human patients, and behold the splendid results!

With what intense satisfaction I show you these splendid results only those who have traversed the thorny path of experience like my own can fully appreciate.

The antitoxin was first used in 1895 and has steadily grown in favor. Now, the physician who does *not* use it and use it speedily is guilty of criminal negligence.

I show you here four diphtheria tables and charts which will repay study.

First, the mortality in cases in which the antitoxin was used on the first day, when not one of 218 cases died; then a rapidly ascending percentage of deaths day by day for the second,

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third, and fourth day. After the fifth day there was a slight decrease for the more susceptible patients had already been slain. The danger of delay is then strongly emphasized.

TABLE I. DIPHTHERIA DEATH-RATE ACCORDING TO DAY ON WHICH THE ANTITOXIN WAS USED

Day	*Cases*	*Death-rate*
1	218	0
2	1153	4.59
3	880	12.50
4	598	16.40
5	351	14.24
After 5th day	694	14.15
	3894	

The second table shows the death-rate per 100,000 of population in New York City at ten years' intervals from 1874 to 1914. Note the sudden and gratifying drop after the antitoxin was first used in 1895.

TABLE II. DEATHS IN NEW YORK CITY FROM DIPHTHERIA

1874	219	per 100,000 inhabitants
1884	136	" " "
1894	158	" " "
1895 Antitoxin Treatment Begun		
1904	57	per 100,000 inhabitants
1914	29.5	" " "

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CHART II

MORTALITY FROM DIPHTHERIA IN FIFTEEN AMERICAN CITIES BEFORE AND AFTER ANTITOXIN TREATMENT

(Original Tabulation, Statistician's Dept., The Prudential Insurance Co. of America)

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The charts I owe to the courtesy of Mr. Frederick S. Crum, Assistant Statistician of the Prudential Insurance Company, in Newark, New Jersey, not, be it observed, a medical man, with a theory to prove, but a man of cold but eloquent figures.

Chart No. II shows, to the left, the mortality rates per 100,000 of population in fifteen American *cities*, *before* the introduction of the antitoxin for diphtheria, and to the right the mortality rates *after* its introduction (1895). The black lines are drawn to a scale of 25, 50, etc. The line of 125 deaths per 100,000 inhabitants is passed by only three cities, Brooklyn 132.3, New York 130.1, and Denver 128.5. The lowest rate is 51.5 in New Orleans.

Contrast with this the rates for the same cities *after* the introduction of the antitoxin. On a similar scale Chicago leads with 38.1 in place of 117, while Washington has fallen from 80.1 to 7.1 per 100,000. *Every* city shows a wonderful fall.

Chart No. III shows the death-rate in twenty *countries* of the world, before (left hand) and after (right hand) 1895. Before the use of the antitoxin Serbia leads with 411.9 deaths per 100,000 of population, then follows

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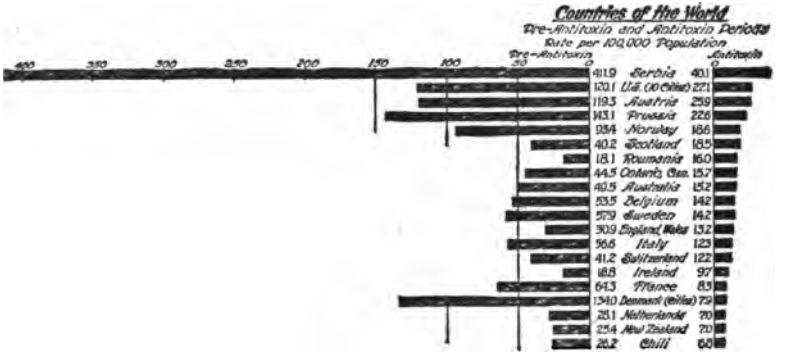
CHART III



MORTALITY FROM DIPHTHERIA IN TWENTY COUNTRIES OF THE WORLD BEFORE AND AFTER ANTITOXIN TREATMENT

(Original Tabulation, Statistician's Dept. The Prudential Insurance Co. of America)

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Prussia with 143.1, Denmark with 134, Austria with 119.3, and the United States with 120.1. Now, look on the right-hand side. The antitoxin has caused a most extraordinary fall in every country. Serbia has fallen to 40.1, Prussia to 22.6, Denmark to 7.9, Austria to 25.9, and the United States to 27.1 instead of 120.1.

The statistics of fifteen American cities and of twenty countries of the world thus present overwhelming evidence of the blessing the antitoxin has brought to all mankind. A conspiracy to "doctor" the statistics and mislead the world is an impossibility. Even if Serbia be discarded, the rest of the tables are sufficiently eloquent.

CEREBRO-SPINAL MENINGITIS

Cerebro-spinal meningitis breaks out occasionally into widely spread epidemics with a mortality of seventy-five per cent or more. Many erroneous diagnoses are made and cases are officially reported to city boards of health as cerebro-spinal meningitis which a more careful and thorough investigation shows not to have been such. The only positively accurate diagnosis is by "lumbar puncture."

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This method was introduced in 1891 by Quincke, of Kiel. The long, slender needle of a hypodermic syringe is thrust within the sheath of the spinal cord in the small of the back — the lumbar region — and a small quantity of the cerebro-spinal fluid is withdrawn. By its examination the diagnosis is made certain.

But as in so many other cases Medical Research does not stop with finding out the cause and making a diagnosis. It rapidly pushes on to the further discovery of a remedy. That is the reason we are always so desperately anxious to find the *cause* of cancer. When that is found we shall be very near to its cure, or better still to its prevention.

The remedy for cerebro-spinal meningitis is a serum elaborated by Flexner at the Rockefeller Institute. This curative serum is injected into the sheath of the spinal cord through the same needle by which the cerebro-spinal fluid is withdrawn for diagnosis and before removing the needle. A single puncture, therefore, answers both for diagnosis and treatment.

"And what," you ask with intense interest, — "what is the result of such a means of sure diagnosis and of the use of such a serum?" With

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pride and joy I reply that the mortality has been cut down from seventy-five to at least twenty-five per cent in most cases, and in some instances to as low as seven per cent. Moreover, apparently an efficient disinfectant for "carriers" of this disease has probably been found.

Do not such results accredit Medical Research with a notable contribution to Human Welfare?

TYPHOID FEVER

Typhoid fever has been one of the historic scourges of armies all over the world. It is a constant cause of many deaths in our civil population, especially in our large cities. The autumnal harvest of deaths from typhoid has been so common as scarcely to cause remark, until of late, when we have learned the lesson of our municipal culpability.

Since Bacteriology revealed the cause and Medical Research discovered the antidote, we have practically conquered typhoid fever in the army and navy. Were the civil population to follow the example of the army and navy there would be few cases of this justly dreaded disease.

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The bacillus of typhoid was discovered by Eberth in 1880. It is so small that it takes 40,000,000 of them to weigh a single grain. (Plate I, Fig. 5.) Like the discovery of the tubercle bacillus two years later by Koch, this was an epoch-making discovery. Practically all of our sanitary precautions, and now our preventive means by vaccination with the anti-typhoid serum, start from the discovery of the bacillus of typhoid.

In the Civil War there were 79,462 cases and 29,336 deaths, a death-rate of thirty-seven per cent — a horrible toll of life! The total number of deaths in the army of the United States in the Civil War was 303,504. Typhoid alone was responsible for nearly one tenth of all deaths!

In the Boer War there were 58,000 cases and 8000 deaths, a death-rate of fourteen per cent. Of the total deaths in that war 22,000 in number from all causes, typhoid caused over one third!

In the Spanish-American War there were 20,738 cases — nearly one fifth of the entire army — and 1580 deaths. Eighty-six per cent of the entire mortality in that short war were due to typhoid!

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A beautiful experiment by Professor Coplin, one of my colleagues at the Jefferson, well shows one of the principal means of spreading the disease in armies. He made a fly walk across a plate of gelatin on which was growing a pure culture of the typhoid bacillus. Then he caused the same fly immediately to walk over the surface of a plate of sterile gelatin. This latter plate was then placed in an oven at a suitable temperature. Wherever the contaminated feet of the fly had touched the sterile gelatin, there a colony of typhoid bacilli sprang up. The footprints of the fly were as evident as the footprints of a horse on a newly smoothed dirt road. (Plate II, Fig. 2.) Any fly which has walked over the infected excreta of a typhoid patient and then walks over the soldier's or our own food carries the infection in like manner. The water-supply, the milk-supply, the fly, and handling food with unwashed hands (how scientific is the Mosaic code in these respects!) — these are the main sources of infection.

Many severe epidemics have been traced to an infected milk-supply — originating, it may be, from a single case of typhoid on the farm or in the dairy.

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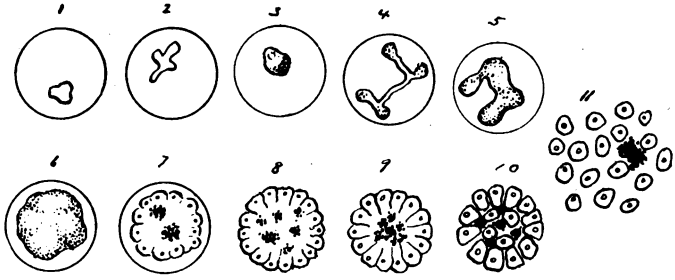

FIG. 1. Different Phases of Development of the Malaria Parasite

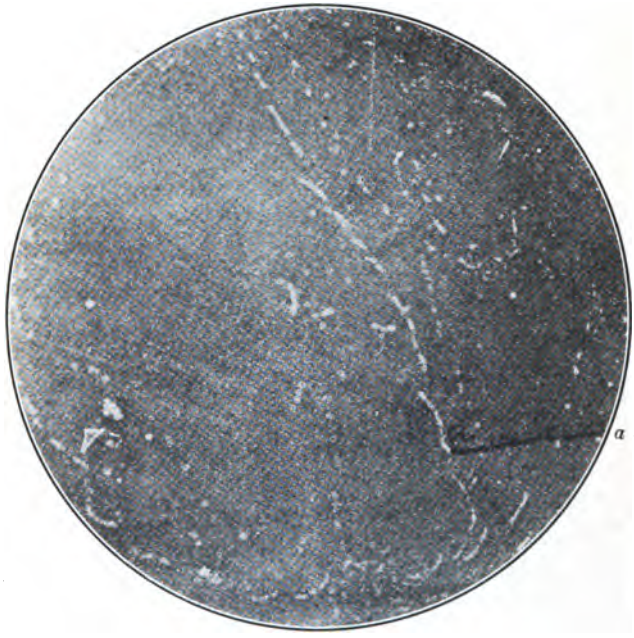

FIG. 2. Typhoid Fly Tracks

Note the left-hand interrupted line (*a*) and the almost parallel dotted line to the right of *a*. The first, *a*, was made by the left wing, the other by the right feet of the fly (see text). Each of these lines represents a row of colonies of typhoid bacilli growing on sterile gelatin infected by a typhoid fly which had once walked over a culture of typhoid bacilli and then once over the sterile gelatin.

PLATE II

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I will only cite one instance of an infected water-supply caused by one single patient. The town of Plymouth, Pennsylvania, was supplied with water from a near-by lake. On a hillside bordering on the lake there occurred in 1885 one case of typhoid fever. This patient's dejecta was thrown out on the snow. When the snow melted in the spring the water ran into the lake. This carelessness in one family caused an epidemic of over twelve hundred cases of typhoid and over one hundred deaths in a population of only eight thousand persons!

Typhoid-carriers, like carriers of cholera germs, are not infrequent as I have already explained. In them the bacilli find a continuing home in the intestines. Wherever these carriers go they leave a trail of typhoid and death.

From the intestines the bacilli of typhoid fever are prone to travel into the gall bladder, where they have been found in pure culture over fourteen years after the fever. They are the cause of dangerous infections of the gall bladder which always require operation.

. But Medical Research — how often shall I repeat this good news! — has not been content with discovering the bacillus of typhoid and

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how this has caused severe epidemics. One of its greatest and most beneficent triumphs has been the discovery of a preventive vaccination with the typhoid antitoxin. The value of this preventive inoculation is best shown by some statistics. I take the following figures from the Annual Report of the Surgeon-General of the United States Army: —

TYPHOID FEVER IN THE UNITED STATES ARMY

Year	*Cases*	*Deaths*
1906	210	12
1907	124	7
1908	136	11
1909	173	16
1910	142	10
Anti-typhoid vaccination made compulsory		
1911	70	8
1912	27	4
1913	4	0
1914	7	3
1915	8*	0

* 4 in the United States; 4 in Hawaii.

The Surgeon-General of the Army calls attention to the fact that "among all the troops . . . on the Mexican border and in Texas . . . *not a single case of typhoid has occurred in an inoculated man since June 4, 1915.*"

The Reports of the Surgeon-General of the

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United States Navy furnish the following similar figures: —

Year	*Cases*	*Deaths*
1909	189	17
1910	198	10
1911	222	15
Anti-typhoid vaccination made compulsory		
1912	57	2
1913	22	4
1914	13	0
1915	15	1

"I have no hesitation in saying," adds the Surgeon-General, "that the practical elimination of typhoid [from the Navy] . . . is due *almost in toto* to this vaccination."

At the beginning of the present European War the armies on both sides were not provided with sufficient vaccine and a considerable number of typhoid cases occurred. By the end of 1915 there were twenty-six laboratories in Germany making the vaccine, and the entire German army had been protected. All soldiers were revaccinated after six months. Many millions, therefore, were inoculated. The "Münchener medicinische Wochenschrift," in May, 1916, stated that not a single death had followed the inoculations. Rarely does any

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serious reaction follow. By December, 1915, there were occasions when, in both the army and among the population of a large town in which the army was quartered, there was not a single case of typhoid.

Up to August 25, 1916, it was officially stated that among the British troops in France the percentage of *deaths* among the men *inoculated* against typhoid was 4.7 per cent; among the *uninoculated* 23.5 per cent. About ninety-five per cent of the soldiers have been inoculated. The percentage of cases of typhoid among the inoculated is, therefore, exceedingly small compared with the percentage of *cases* among the uninoculated.

The latest and still more remarkable typhoid statistics were presented in the House of Commons on March 1, 1917, by Mr. Forster, as follows: The last weekly returns showed only twenty-four cases in the four British Armies in France, Salonica, Egypt, and Mesopotamia. He added that "the total number of cases of typhoid fever in the British troops in France down to November 1, 1916, was 1684, of para-typhoid, 2534, and of indefinite cases, 353, making a total of 4571 of the typhoid group."

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In the Spanish War in 1898 (see table below) every fifth man contracted typhoid fever. If the same ratio (1 to 5) had held in the British army alone in the present war there would have been 1,000,000 cases! The actual number has been less than one case in every *thousand* men instead of one in every *five* men.

It may be truthfully said, "Typhoid fever in war has practically disappeared." At the beginning of the present war Germany had provided many large hospitals for the expected typhoid cases. These hospitals have never been filled. Most of them have been used for other purposes. Look at the extraordinary contrast between the typhoid record of the four principal wars of the latter half of the nineteenth century and the present war. Nothing could possibly be more convincing. Research has conquered typhoid.

TYPHOID FEVER IN FIVE WARS IN FIFTY YEARS

	Cases	*Deaths*
Civil War, 1861–65	79,462	29,336
Franco-Prussian, 1870–71	74,205	8,904
Spanish-American, 1898	20,738	1,580
Boer War, 1899–1902	58,000	8,000
War of 1914–16	Almost none (see text) when compared with the millions engaged	

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In our civilian population the story is very different. There has been a great improvement from 1900 when the death-rate was almost 40 per 100,000 — reduced to 12.4 per 100,000, or only one third as many, in 1915. But then there were over eight thousand deaths from typhoid in 1915 in the registration area of the United States, which contains only two thirds of the entire population. For the whole country, therefore, the deaths were approximately over twelve thousand. Had there been universal civilian vaccination I doubt if there would have been five hundred deaths instead of twelve thousand. Twelve thousand deaths mean also certainly largely over one hundred thousand cases of anxious and expensive illness, almost all of which would have been prevented.

TYPHUS

Not long since I listened to the story of the conquest of typhus fever in Serbia as told by Dr. Richard P. Strong, of Harvard. My wonder grew from sentence to sentence as he recounted the ravages of the fever, the obstacles to be overcome, the scant weapons he had with which to fight the fever, and yet he and his

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splendid band of doctors and nurses surmounted every difficulty and won a great victory. Imagine the situation — a whole nation, half famished, half clothed, infested with lice, thousands of patients to be fed, disinfected, cleansed, re-clothed, and nursed through a long illness in few and ill-furnished hospitals, with no clean potable water to be had, and a lamentably small staff of nurses. The whole civic life was destroyed; the military necessarily predominated. Not the least obstacle was the difficulty of utilizing an unknown language. Yet even amid all war's alarms, he and one of my old Jefferson boys and their colleagues and heroic nurses finally banished typhus. But the grim fever had its reprisals. Death claimed its toll of not a few of the finest of those brave doctors and nurses.

Typhus fever, or, as it is variously called "ship fever," "jail fever," "hunger fever," — ominous names, — at times has been a veritable pestilence, destroying thousands. Its cause was entirely unknown and its mode of transmission most obscure until modern science discovered them.

In 1909 Anderson and Goldberger in America, and Nicolle in Algiers, independently dis-

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covered that the body louse becomes infected by feeding on the blood of typhus patients and in turn infects humans by its bite. How difficult a problem the destruction of the body lice was may be imagined from the statement of Dr. Hall, Texas State Quarantine Officer, that the physician should wear silk underwear, as the louse will not deposit any eggs on silk, and should take three baths a day, the last being of gasoline. The lice will outlive even washing with soap and water — often, I fear, also a severe and novel ordeal for the Serbian patients.

Among the Americans who have confirmed this discovery I wish to mention with especial honor two of our fellow-countrymen, Drs. Conneff and Ricketts. At the threshold of most promising careers they fell at their posts, and have added two more names to the martyr-roll of science. They fully understood their great danger, but they cheerfully made the great sacrifice.

Plotz, of New York, has probably discovered the germ of typhus and, in conjunction with Olitzky and Baehr, has possibly found an antitoxin. In Serbia, Bulgaria, and Volhynia, 8420 persons, especially those most exposed to the infection, were inoculated with this anti-

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toxin, and during the four months of the epidemic only six fell ill with typhus and only two died. If further observations confirm this discovery another laurel crown will adorn the brow of Research Medicine.

MALTA FEVER

The story of the elimination of Malta fever from the British army and navy and the native inhabitants of Malta is a striking example of the benefit conferred by Medical Research.

That lovely island in the Mediterranean, famous in the Scriptures, in ancient history, in the legends of the Crusades, and in modern military geography and strategy, should be one of the healthiest spots on the globe. Yet a peculiar fever was so common as to have received its name from the island. Assignment to duty there was feared alike by the men and the officers. Indeed, it was more feared by the officers and their families than by the men. Clean, airy quarters, excellent sanitation, far from preventing seemed to invite the fever, for in the officers' quarters it attacked three times as many proportionately as among the men in crowded barracks. Among a garrison of seven

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thousand soldiers there were an annual average of three hundred and twelve cases and in the navy a similar proportion. As late as 1905 there were 643 cases. The illness was a very painful one with great emaciation and weakness. Very many had to be invalided home.

The germ is an extremely minute organism and was supposed to be borne by the air. In 1904, aroused by the ravages of the fever, the Royal Society sent a commission to investigate. They examined exhaustively the climatic conditions, the water-supply, the drainage, the water in the harbor, the slums, the various kinds of dwellings and their possible defects. Then the air was examined. The mosquito was found to be guiltless. Finally, the food-supplies were investigated, and at the end of three years' steady work they discovered the way in which perfectly healthy people living in almost ideal conditions became infected, and at once the disease vanished.

Among other foods the milk-supply was examined. This was furnished by about twenty thousand goats. These goats, like the mosquitoes and the various "carriers" already described, were apparently perfectly healthy, and, therefore, for a long time had escaped sus-

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picion. The milk of some thousands of goats was examined. One half of them were infected and in a large number of them the milk was full of Malta fever germs. Monkeys fed on the milk for one day fell ill of the fever. Even one drink of infected milk would give it to a human patient. Goats' milk was then prohibited. Note the result. In 1905 there were 643 cases. In 1907 there were only seven cases. From 1910 to 1913, in four years, there were only twenty-two cases in all, all traced to goats' milk. Some of these few had not been infected in Malta, but were immigrants from other infected places.

In 1911 Gentry and Ferenbaugh, in southwestern Texas, discovered Malta fever on some great ranches and confirmed its origin from the goats.

TETANUS

What a world of terror is contained in that one word — "Tetanus!" "Lockjaw" is the popular name for it because the earliest symptom is a difficulty of moving the lower jaw. The stiffness soon increases so that it is impossible for the patient to open his mouth —

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hence the name "lock-jaw." But the disease does not stop there. The spasms, first manifested in the muscles of the jaw, spread all over the body and may become so severe as to bend the body backward like a bow so that in severe cases the sufferer only touches the bed by his heels and his head. A robust arm can be thrust under the arched body without touching it.

Never shall I forget a fine young soldier during the Civil War who soon after Gettysburg manifested the disease in all its dreadful horror. His body was arched as I have described it. When at intervals he lay relaxed, a heavy footstep in the ward, the bang of a door, would instantly cause the most frightful spasms all over his now bowed body and he hissed his pitiful groans between tightly clenched teeth. The ward was emptied, a half-moon pad was hung between the two doorknobs to prevent any banging; even the sentry, pacing his monotonous steps just outside the ward, had to be removed beyond earshot.

You have all experienced the severe pain of strong cramps in the calf of your leg or sole of your foot, and know how almost unbearable a severe cramp becomes so that you even may be

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obliged to cry out. Imagine, not the calf muscles only, but every muscle of your head, neck, body, arms, fingers, legs, toes, gripped in cramps ten, twenty-fold more severe. Moreover, what makes one shudder the more is the fact that, as in this poor young fellow's case, his mind was as clear as yours or mine at this moment. Nothing lessened or even blurred his capacity to feel the horrible pain. The spasms became more and more severe, the intervals shorter and shorter; it did not need even a footfall now to produce the spontaneous cramps, until finally a cruelly merciful attack seized upon the muscles of his throat and then his body was relaxed once more and forever. He had been choked to death.

The first time I saw the statement in a medical journal that lockjaw was of telluric origin I recall vividly my entire incredulity. That it came from the ground, the earth on which we walked, seemed to me incredible. We had known for many years that hostlers and others who worked among animals, especially horses, were far more often attacked, and everybody was familiar with lockjaw as a result of treading on an old rusty nail. These were undoubted facts, but no one knew the reason for them.

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Finally, in 1884, Nicolaier demonstrated the curiously shaped bacillus like a tack or a drumstick. (Plate I, Fig. 6.) Then it was found that the bacillus infested the intestines of the horse and other animals. Yet, strange to say, here is another instance of a microbe which is entirely harmless to its host, the horse, so long as it is limited to its normal home, the intestines, but once let it get into a wound, even of a horse, and it is deadly: tetanus develops and with a terrible mortality both in men and horses. In the Civil War the mortality was just short of nine out of every ten patients. We now understand why such a large number of cases of lockjaw were seen at the beginning of the present war. France and Flanders had been roamed over by animals ever since before the days of Cæsar's Gallic War, and the ground was saturated with the tetanus bacilli. The soldiers in the trenches had the earth grimed into their clothing. It coated their bodies. When hit by a piece of shell, a bit of clothing or of their muddy skin was driven deeply into the wound and with it the germs of tetanus.

Our Fourth-of-July tetanus tells the same story and well shows another feature of this special bacillus. Some germs grow best in the

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air with plenty of oxygen. We call them air-living, i.e., aërobic. To others oxygen is an enemy. They grow best without air; i.e., they are named an-aërobic. The germ of tetanus is one of the anaërobic kind. When the small boy is wounded by the little bullet of the toy pistol, or when he steps on a rusty nail on the highway, a little blood escapes for a few minutes, then clots, soon dries, and so completely closes the little wound. The oxygen no longer can get access to the interior of the wound. The conditions are ideal for the tetanus germs to grow. The poison reaches the nerves in the wound, travels to and then up the spinal cord, and soon every muscle in the body is in the horrible spasms.

But Medical Research again has elaborated an efficient preventive. The prohibition of the toy pistol has greatly lessened the number of cases and the practically universal use of the antitoxin as a preventive in all well-equipped hospitals has almost given the *coup de grâce* to Fourth-of-July tetanus.

The Great War has triumphantly established the value of the antitoxin. At first, when the supply of antitoxin was wholly inadequate for such huge armies, there was a considerable

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number of cases of tetanus. But now for a long time there has been an ample supply of the antitoxin. As every wound is an infected wound and every case may develop lockjaw, every wounded soldier at the very first practicable moment is given a full preventive dose of the antitoxin by a hypodermic syringe. The result is that while no actual percentages or figures have been published, tetanus, it is stated, has almost disappeared. At the Second German Surgical War Congress in April, 1916, the President declared that, in the year just passed, tetanus had been "completely suppressed" in the German army. The wounded who have lain between the lines for hours or even a day or two are liable to develop lockjaw, but the men who promptly received a hypodermic of antitoxin go practically scot-free.

What a happy — indeed, one may say what a splendid — result from Medical Research!

LEPROSY

Dr. Victor G. Heiser, I hope, may be the conqueror of leprosy.

We are all familiar with the pathetic cry in the Book of Books, "Unclean! Unclean!" Well

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does the repulsiveness of its victims warrant the cry. Though originally only a disease of the Orient, it has slowly spread all over the world. We have a considerable number of cases in the United States.

The first step in its eradication is segregation. Heiser — who was the efficient Director of Health of all the Philippines for ten years — persuaded practically all the lepers in the Philippines voluntarily to go to the Island of Culion, where he built a town, officered, policed, cleaned, and amused by lepers. They have even their own currency (a token currency for use only in Culion itself), a town hall for plays, lectures, — "movies," I feel sure, — and other recreations.

This segregation prevents any new cases from arising by contact. Chaulmougra oil has long been known as a remedy which has greatly benefited leprosy, but never cured it, since the stomach after a time revolts and the patient can no longer take it. Heiser has discovered a means by which the oil can be given hypodermically and continuously. The treatment requires over a year — sometimes two years. When I last saw Dr. Heiser he told me this oil was being used in many places in the East, that two score patients had remained well with-

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out treatment for two years, and that very many more were on the way to cure.

As a result of this favorable outlook, the Rockefeller Health Commission has sent Dr. Heiser all around the world to obtain the co-operation of various governments in this treatment of leprosy, and at the same time in the cure of the hookworm disease. If, as seems probable, he can obtain this coöperation, he is strongly inclined to think that the eradication of leprosy and hookworm disease is a possibility.

INTERNAL SECRETIONS AND THE DUCTLESS GLANDS

I must now ask your close attention to a very obscure subject even to medical men. Yet it is a subject of intense interest and vital importance, the knowledge of which has been forced upon the profession in the last twenty years. I mean the internal secretions and the ductless glands.

The liver, the pancreas, the kidneys, the salivary and other similar glands discharge their secretions by tubes called "ducts," by which their secretions reach the intestines, the bladder, the mouth, etc. In 1848 Claude Bernard

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discovered that the liver not only secreted bile, which was passed into the intestines through its duct, but that it had a second function. It secreted sugar, which was discharged, not by any duct, but into the blood itself as it passed through the liver. This was a wholly new idea — that any organ could produce two secretions, one discharged through the duct and the other added directly to the blood.

But while this discovery caused a great sensation in the scientific world, the idea that there might be a number of other glands, which, having no duct, produced only the second sort of secretion which reached the venous blood in its course through these glands, was scarcely entertained.

In 1873 Sajous, of Philadelphia, insisted on the existence and importance of these "internal secretions," as they were properly called, but the greater part of medical men were inclined to think the idea rather fantastic and did not take it seriously. Meantime a few men were experimenting especially on the thyroid gland in the neck, a gland the enlargement of which you all know as a "goiter." They found that its internal secretion played an important part in the animal economy, as I shall show you.

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Finally, as Adami says, "the doctrine of internal secretions . . . came into its own" by the convincing experiments of George Murray on the thyroid in 1895. [The best recent book — and a very remarkable one — is "The Thyroid Gland in Health and Disease," by Robert McCarrison, London, 1917.]

"All this seems, no doubt, interesting to the physiologist," you say, "but is it really of any fundamental importance to us?" In reply let me relate a personal experience — one of those terrible tragedies of surgery which unavoidable ignorance inflicted upon me.

In 1890, after I had long practiced antisepsis and in this particular case had used every precaution known to science, I removed the thyroid gland for a large goiter. Everything went well during the operation and for twenty-four hours afterwards. Then set in what is called "tetany." The young woman became restless, constantly tossed about, could not sleep, became excessively excitable, at times almost maniacal, and death quickly followed. Never have I been able to banish the bitter recollection, which even now at times surges up in my mind, that I was unwittingly her executioner. No one who has not gone through such

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a heart-breaking sorrow can know its wearing grief.

One year later — too late, alas! to be of benefit to her or to me — the fact that tetany, following an operation for goiter, is due to the removal of the little "parathyroid glands" was first demonstrated by Gley. These little glands, which I had ignorantly removed, were only discovered in 1880 by Sandström. They consist of two, three, or four oval bodies lying closely behind the thyroid gland. They are with difficulty distinguished from it. They are only one quarter of an inch long, yet they are essential to life. This has been demonstrated by their intentional removal in animals, and their unintentional removal in human beings as in my case. If one or two are left, the patient can live, but removal of all is surely fatal. But when I performed the operation just described, all of us were utterly ignorant of their vast importance. In fact the idea seemed almost absurd that such insignificant little bodies, scarcely seeming to be more than masses of fat no larger than a small pea, *could* be of any serious importance. But as I have shown you, life and death hung upon the knowledge of the function of these parathyroid glands.

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Now, having learned their supreme importance we have also learned how to avoid their removal and thus to avoid a fatal error.

How else can we learn the terribly important function of these little glands except by experiments on animals? Even now their exact physiological influence is too uncertain to make any positive statement advisable beyond that already mentioned, that the removal of all of them is fatal. Is it not a duty to learn all we can about them as quickly as possible, and not only to learn all we can about the parathyroids, but about all the other ductless glands as to which we still know so little?

Do you wonder that we surgeons, physicians, physiologists, and obstetricians yearn intensely, yea, with all our souls, for "more light," so that we shall not innocently and in fact unconsciously sacrifice the lives of our patients that is, of you and your children?

What a chapter could be written on the "Calamities of Unavoidable Ignorance!"

What are the glands of internal secretion? There are two very large glands of double secretion, the liver and the pancreas. They secrete respectively bile and pancreatic juice. These secretions reach the upper intestine di-

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rectly through their regular ducts and are essential to normal digestion. Both of these two great glands also have an internal secretion which escapes directly into the blood and assists in the transformation of sugar into alcohol and carbonic acid.

The spleen is also a ductless gland, but in spite of its size, as large as a fist, it is not essential to life. It has been successfully removed many times. But I pass it by simply because we know so little about it, and that in spite of constant study and experiment.

The other ductless glands with one exception are all very small. The smallest seem even to be the most important. Some are single and lie in the mid-line of the body. They comprise, first, the pituitary gland, or "hypophysis," at the base of the brain and about two and a half inches back of the root of the nose. The name "pituitary" is derived from the old erroneous notion that it secreted the "pituita," the Latin term for the nasal mucus. That we now know comes from the nasal mucous membrane.

Next comes the pineal gland, again at the base of the brain and about four to five inches back of the root of the nose. This gland was

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again erroneously declared by the older anatomists to be the "seat of the soul." Its function — and it surely must have one — is practically unknown to us.

A third is the thymus gland, situated just behind the top of the breast-bone. This is only a temporary organ. It is about two inches long and at birth weighs half an ounce. It enlarges somewhat during the first two years of life, then ceases to grow, and at about the period of puberty rapidly shrivels up, but never wholly disappears. Its function is very obscure, but it ministers in some unknown way to the needs of the body, especially as to development and growth up to the age of puberty. During early childhood it is sometimes the seat of a rare but serious and sudden change which is almost always rapidly fatal.

Its removal in animals impairs the development of the bones especially due to a diminished amount of phosphate of lime. A condition like rickets ensues, the bones easily bend, and are readily fractured. Its removal in hens causes them to lay eggs without shells. If a fresh thymus is re-implanted in animals from which the original thymus was removed, the normal processes are restored. In idiots the thymus is

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generally absent, as is shown by *post-mortem* examinations.

Other ductless glands are bilateral, e.g., first, the parathyroids, of which I have already spoken.

Secondly, the adrenal or supra-renal glands are also bilateral and are of great importance. They are situated one at the upper end of each kidney. Of these I shall speak later.

A few other glands of internal secretion exist. Some, seemingly unimportant, of whose function we are at present wholly ignorant, may easily be found to be of great importance when we really learn their uses. Certainly they cannot be found in human beings and many animals and yet be useless.

But I must ask your further close attention to some of the results of Medical Research as to the thyroid, the pituitary, and the adrenal glands. These are of great interest and of great practical importance. The pituitary, the parathyroids, as I have already shown, and the adrenals, all three are absolutely essential to life and the thyroid is essential to normal life.

Lack of the normal secretion of the thyroid gland when it is congenital — that is, existing from birth — gives rise to the condition called

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"cretinism," amounting almost to idiocy. When it occurs in adults, it causes a condition called "myxedema"— a degenerative condition of mind and body.

In these conditions of *too little* of the internal secretion of the thyroid gland, attempts have been made — and in not a few cases with brilliant success — to supply the deficiency by administering an extract of the thyroid glands of sheep. This is a notable contribution of Medical Research to Human Welfare.

The same extract has been used in cases of apparently normal young persons, whose physical growth, however, has been retarded for some unknown cause.

The most remarkable instance I know of its benefits — a wholly exceptional case — was recorded by Dr. George A. Gibson, of Edinburgh, just before "the curfew of his life was to quiver on the evening air," to use his own poetic and prophetic expression. If I had not known him well personally and could vouch for his scrupulous exactness, I should be disposed to think him rather careless of the truth.

A lad of eighteen, who had set his mind on entering Woolwich, the English West Point, was only four feet and eleven inches in height.

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This was four inches below the required height and the examination was only six months away. The case seemed hopeless, yet following the administration of thyroid extract, under Gibson's careful supervision, in six months the lad grew seven inches in height! And what was most gratifying, his mental development was not in the least interfered with, as he attained high rank in his classes. But such a powerful remedy must never be used except under continuous medical care.

When there is an *excessive* secretion from the thyroid gland there results that especially dangerous form of goiter known as "exophthalmic goiter" or "Graves' disease."

The pituitary gland or hypophysis is only as large as the tip of the little finger and weighs only seven to eight grains. Small as it is, it is divided physiologically into a front, middle, and back portion, differing anatomically and physiologically.

The front part is essential to life. Its removal is quickly fatal. When diséased, it causes the overgrowth of the bones, especially of those of the face and the extremities, a condition which not very seldom develops in adult life and is known as "acromegaly." Very slowly

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the bones of the face become leonine, or greatly enlarged, as do also those of the fingers and toes.

The secretion of the middle and back part activates the heart and stimulates the kidneys and the milk glands. It also lessens the caliber of the blood vessels and thus influences the blood pressure in a manner similar to the secretion of the next glands to claim our attention.

The adrenals are two glands lying on the upper end of the two kidneys, and hence called "ad-renal" or "supra-renal" glands. They are slightly larger than the last joint of the thumb. Their secretion is called "adrenalin" or "adrenin." These glands have been known ever since 1564, but our accurate knowledge of their function and the chemical isolation of their secretion goes back less than a score of years.

Their active principle or secretion was first isolated in 1901 by Takamine, a Japanese working in New York. It is constantly being secreted in small amounts. It keeps up the normal tone of the blood vessels and the normal percentage of sugar in the blood. How extraordinarily powerful it is, is shown by the fact that a solution of one part in 200,000,000 — that is, one drop in one hundred barrels of water — when applied to the intestine of a living rabbit

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is sufficient to stop the movements of the intestines! It increases the activity of the heart. It shifts more or less blood from the great blood vessels of the abdomen — note this with care — to the *heart, lungs, muscles,* and *central nervous system.* This enables the body as a whole to respond to sudden physical and mental emergencies, requiring quick action and unusual exertion, for fight or flight — an "emergency function" as Cannon well names it. Thus fear, rage, or pain causes instant and unusual pouring out of adrenalin and mobilizes our physical and mental forces for use in such emergencies.

This influence of fear, acting on the adrenals, the thyroid, and possibly the liver, is, I think, the explanation of the unusual phenomena in the case of a little girl nine years old under my care some years ago in the Jefferson Hospital. She weighed about fifty pounds. A year earlier her clothing had caught fire and she had been dreadfully burned. I was obliged to amputate her left arm at the shoulder joint. She quickly recovered and was waiting to go home. One night a large fire broke out, only a block away; the flames were visible through the great windows of the ward, and flooded it with light. She woke up suddenly screaming with

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terror, thinking that the ward was afire and that her former terrible accident might occur again. Her temperature, which had been normal for days, had suddenly risen to 104.5° F. All her forces of mind and body were mobilized for escape. After a time, when her fears were quieted, she fell asleep. In the morning her temperature had fallen to normal. Her adrenals had raised the temperature of her fifty pounds of flesh six degrees in almost as many minutes!

Adrenalin is now frequently used in surgical operations to raise the blood pressure when danger threatens from loss of blood and shock.

The experimental methods by which the functions of these various glands have been discovered are chiefly by removal of part or all of a gland if it is single, or by removal of one or more if multiple, and then observing the results. These vary when the experiment is done on young, growing animals and on adult animals. Such experiments are obviously utterly impossible in man. Occasionally also cases occur in humans and animals of tumors of these glands or of degenerative processes, which add to our knowledge.

By many experiments and observations two other facts have been ascertained.

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First, that the glands of internal secretion, about which we really know as yet but little, are all more or less closely interrelated and form a complex system of their own. Some day we may hope to understand this system completely, instead of very imperfectly as at present. This interdependence is well known by a clever experiment, again not possible in man. It has an undoubted significance which is as yet not understood. The small amount of adrenalin normally poured into the blood evokes a marked current of electricity in the thyroid gland. Clamping the veins from the adrenal glands, thus preventing the return of the venous blood from the adrenals, containing, of course, this small amount of adrenalin, into the general circulation immediately stops this current of electricity. When the clamp is removed and the venous blood containing the adrenalin again reaches the general circulation, the electrical current promptly reappears.

The second and very recent discovery is the existence in the secretions of these ductless glands of what are called "hormones"; i.e., "stimulators" or "excitors." These substances, secreted by one gland, stimulate other, distant, and apparently wholly independent,

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glands into activity. In fact, without the secretion of gland number one, gland number two cannot function. If disease prevents the secretion of the hormone by gland number one, the function of gland number two is altered or abolished. Is it not strange, passing strange, that the human body, "a harp of a thousand strings, should keep in tune so long?"

Several of these hormones or excitors are now known, but we are only at the beginning of such researches.

I have dwelt at greater length and in greater detail on these curious glands because several of them, as I have shown you, are essential to life, because the researches into their functions well illustrate the methods of Medical Research, and finally, because, if even our very imperfect knowledge has been of much benefit to man, it is evident that complete knowledge will be far more useful.

MEDICAL RESEARCH IN DISEASES OF ANIMALS

I have far too little time left for the researches into the diseases of animals. These diseases seriously affect Human Welfare, for

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they often attack humans and destroy their lives. They cause enormous economic losses to the community, as I shall show. They lessen the number of our draft animals. They diminish seriously our food-supply of meats, fats, milk, butter, cheese, and eggs, and affect the supply of wool and hides for our clothing. Finally, they diminish our recreations and our pleasures.

Five thousand millions of dollars are invested in domestic animals in the United States. In 1912 there were lost six and a half millions of swine, two millions of cattle, two and a half millions of sheep, and half a million of horses and mules. Reflect also for a moment on the sufferings inflicted by relentless Nature upon these millions of animals which Medical Research is endeavoring to mitigate or abolish!

The Department of Agriculture in 1915 computed the following astonishing table of the direct *annual* losses from animal diseases in the United States simply in terms of money value, to say nothing of the sufferings of these patient animals, of the dangers to human life, or of our diminished food and our clothing supplies: —

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DIRECT ANNUAL LOSSES BASED ON RETURNS FOR THIRTY YEARS FROM ANIMAL DISEASES IN THE UNITED STATES

Hog cholera	$75,000,000
Texas fever and cattle ticks	40,000,000
Tuberculosis	25,000,000
Contagious abortion	20,000,000
Blackleg	6,000,000
Anthrax	1,500,000
Scabies of sheep and cattle	4,600,000
Glanders	5,000,000
Other live stock diseases	22,000,000
Parasites (trichina and others)	5,000,000
Poultry diseases	8,750,000
	$212,850,000

The chief diseases of animals which man is in danger of contracting are anthrax from sheep and cattle, hydrophobia from dogs, wolves, coyotes, etc., the trichina parasite in pork, glanders from horses, and tuberculosis from cattle.

Hydrophobia, anthrax, and other similar diseases I have already considered in tracing Pasteur's wonderful career. Fortunately anthrax is the least destructive of all those named in the above table. In man it is rare in the United States. Personally I have seen only one case.

The *trichina spiralis* is well known to all

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intelligent people. It was first discovered by Richard Owen eighty years ago. Its life history was fully studied by Virchow in 1865–66 when I was a student in his laboratory.

It is a spiral worm which encapsulates itself in the muscles of swine. When pork is eaten raw by man, the gastric juice dissolves the capsule or envelope, sets free the worm, which then finds its way to the muscles and other organs, even to the brain, and often destroys life.

For years our Government has had extensive and expensive laboratories in order to examine with low-power microscopes all our hog, cattle, and other exports for trichina, tuberculosis, etc. How enormous and also how imperative this work is we appreciate when we learn that in 1916 the Bureau of Animal Industry reported that over 62,000,000 animals were examined in 875 laboratories in 247 cities by 2554 employees; 11,800 live animals and 738,000 parts of carcasses were condemned. The condemned carcasses and parts were destroyed or converted into fertilizers.

Without this inspection such exports are barred out of other countries. Our own citizens are far more exposed than are foreign consum-

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ers, for state and city inspection is often ineffective and sometimes non-existent. "Country sausage" may easily be less certainly safe and wholesome than if made in a city which enforces a proper inspection. Happily, in this country we almost never eat pork products raw, as is common in Germany and hence our people suffer but little damage to health and life. Thorough cooking kills the parasite and removes the danger.

But for commercial purposes Medical Research has shown that the microscope is not a complete protection from the trichina, for only small fragments of tissue from the several places where the parasite is usually found are examined. Latterly the Department of Agriculture has found that freezing, i.e., cold storage at 5° F. for twenty days kills the worm. This method reaches the parasite wherever it is located, is far more effective, and also less expensive than the microscopic inspection hitherto in vogue. But even then I personally would prefer to "make assurance double sure" by thorough cooking — employing both freezing and fire to make a trichinous purgatory.

But until Medical Research discovered the parasite, learned by experiment its life history,

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and discovered the means of prevention, many human lives were sacrificed.

TEXAS OR TICK FEVER

Though not contagious for men this deserves mention for two reasons. First, it ranks second in the table of economic losses to our country, being responsible for a loss of $40,000,000 a year, and by so much also it reduces our food-supply. In both these ways it affects human health and human welfare. In addition to this it is notable as the first disease which, by experimental research, was discovered to be an "insect-borne disease." In 1889 Dr. Theobald Smith read a paper describing most lucidly the experiments by which he had discovered the cause of this fever and the mode of its transmission. His experiments were made by pasturing healthy cattle in enclosed fields on which cattle which had died from Texas fever had been pastured, just as Pasteur, you will remember, investigated anthrax. The healthy cattle in turn soon fell ill and died. His experiments took place ten years after the first book on medical thermometry had been published, and Smith points out that if the thermometer had

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not been used, the rise in temperature, its earliest symptom, would have entirely escaped notice. He found in the blood, liver, and other organs the parasite which caused the fever. Smith and Kilbourne then discovered the mode of transmission. That ticks were the medium had long been suspected. They proved it.

They bred ticks in captivity. The eggs hatched out normally, but, strange to say, it was found that the insects failed to develop unless placed on cattle, their special foster-parent, so to speak. The young ticks just hatched out at first were not placed on cattle. They were watched from December to May, and during all this time they merely lived, but did not grow. In May, the moment they were placed on cattle, they began to develop, and the first moult took place within a week. Three weeks later and after a second moult, the tick falls to the ground and dies after laying from one thousand to two thousand eggs. In two weeks or more the new ticks are hatched and again seek the cattle and the cycle begins again. When the disease reappeared, the second summer of Smith's experiments, — this remember was almost thirty years ago, — like a flash the conviction came to him that he had

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witnessed a new fact, the rôle of insects in the causation of disease.

After the tick had infected the cattle, the parasite begins the second phase of its life inside the blood corpuscles of the cattle. The red blood cells are destroyed by millions upon millions daily and death soon follows. In acute epidemics the disease kills from ten to ninety per cent. Besides this it lessens the value of the survivors, and retards their growth in size and weight. The ticks are killed by "dipping" the infected animals in an arsenical preparation. A tick-infected steer weighing 730 pounds when thus cured gained in two months 385 pounds in weight with a corresponding increase in value to its owner and to our dinner tables.

The infected areas of land are so large that widespread quarantine over the infected areas is still required. Since inspection began over 284,000 square miles have been released from quarantine, being free from infection, but 253,000 square miles are still under the ban. This shows what a huge task our Bureau of Animal Industry still has on its hands in this one disease alone. Millions of cattle have to be inspected every year; over sixteen and a quarter millions were examined last year.

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As this was the first disease which was proved to be spread from one animal to another by an insect, it strengthened the suspicion that the mosquito might harbor the parasite of malaria, and later that yellow fever was spread in a similar manner. Now we know not only that these diseases are insect-borne, but that the tsetze fly carries the fatal sleeping-sickness of Africa, that lice spread typhus fever, and fleas spread the plague.

These studies by Smith and his associates, followed by those of the American Yellow Fever Commission, proving that mosquitoes carried malaria and yellow fever, not only contributed enormously to the welfare of man and animals, but made the Panama Canal a possibility. What an imposing by-product!

What a satisfaction it is that the Rockefeller Foundation has given a million, with more to follow, to carry on their splendid studies in animal diseases and has placed at the head of this department Theobald Smith, the most distinguished living student and discoverer in animal diseases.

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HOG CHOLERA

This fatal disease ranks first in the table of losses from animal diseases in the United States, being responsible for an annual loss of $75,000,000. This huge diminution of our food-supply is one of the reasons for the high cost of living. It is a highly contagious disease, having frequently a mortality of seventy to eighty per cent; sometimes every hog dies.

The cause of the disease is one of those strange germs so difficult and even impossible to find or to cultivate. They are so small as to pass freely through the finest filters which prevent the passage of the vast majority of germs, such as those of typhoid, diphtheria, etc., small and microscopic as the latter are. Yellow fever, smallpox, hog cholera, foot and mouth disease and contagious pleuro-pneumonia of cattle are probably all caused by similar germs so small that it may be a question whether we ever can see them. By inoculation experiments, however, we are learning gradually very much about them. After a while we shall certainly discover and as certainly vanquish them.

Even now Medical Research has found a

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serum against hog cholera which costs but twenty-five cents a dose. Field tests have proved its value and we may look with confidence to the future.

In two thousand hogs on forty-seven farms treated with this serum, eight-five per cent of the hogs which sickened were saved. Of other hogs in the same herds but untreated, only twenty-five per cent escaped. After inoculation with the serum, herds exposed to contagion were all saved. In three selected counties the mortality in 1912 was 28.4 per cent; in 1913, in these same counties, the use of the serum cut down the mortality to one fourth (7.7 per cent), and in 1914 to one seventeenth (1.7 per cent). Meantime the number of hogs had increased over seventy-five per cent.

But I must omit other researches in diseases of animals of the greatest interest and of equally great importance, such as glanders in horses, foot and mouth disease (a very fatal disease of cattle), contagious pleuro-pneumonia, etc., all of which seriously diminish our supply of food and clothing. I must also omit all the diseases of fowls which occasion great loss and again greatly diminish our poultry and egg supply.

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RESEARCH IN DISEASES OF PLANTS

Bacteria in Soil and Rocks

This subject is exceedingly wide. You see with sadness the destruction of our elms and chestnuts and many other trees by fungi and various other pests. Even as I write, the "white pine blister disease" is threatening to destroy our white and five-leaved pine, with a loss of $350,000,000. You know only too well the many destructive moths which have cost millions even to diminish their ravages, to say nothing of exterminating them, which so far has been impossible. These losses are not only economic, but esthetic as well.

Our knowledge of the bacterial origin of plant diseases began in 1878 when Burrill announced the bacterial origin of pear blight. Twenty years ago, with prophetic vision, Dr. Erwin F. Smith declared that "there are in all probability as many bacterial diseases of plants as of animals." The realization of this prediction is well shown by a paper of Dr. Surface, of the Pennsylvania Department of Agriculture. In 1916 he described sixty-eight separate enemies and thirty-eight separate diseases attacking twenty-four grains, plants, and vege-

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tables. It is no wonder that our farmers have suffered such serious losses. If all these diseases could be mastered, how enormously would our food-supplies be increased and the cost of living be decreased. Only by incessant and intelligent research can this be accomplished.

As I am correcting this proof, the world-wide shortage of food and the consequent danger of hunger and even famine in belligerents and neutrals alike, and even for a time after the war stops, strongly reënforce all I have said as to the imperative need of Research.

Plant bacteria resemble animal bacteria in almost every particular. They obtain entrance through wounds — in Italy not seldom through wounds of the olive caused by hailstones — some are aërobic; some anaërobic; some attack old tissue, some young; some are water-borne and some insect-borne; some produce gas; they react to stains; they are variously colored, and they have a geographical distribution.

I can consider only three aspects of this broad problem.

I. Bacteria in the Soil

By the researches of Wilfarth and Hellriegel in 1866 and of Schloessing and Müntz

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in 1878 it was shown that nitrification of the soil was accomplished by bacteria. Plants require nitrogen, of which there is abundance in the air, for eighty per cent of the air consists of free nitrogen. Plants, however, cannot use this free nitrogen. They must obtain it from its combinations in ammonia and nitrates.

There are "bad bacteria," as shown by Pasteur in puerperal fever, the diseases of wine and beer, etc., and by Lister in the infection of wounds. But there are also "good bacteria." Decomposition is due to bacterial action. Stable manure — a typical form of decomposition — is valuable because of this ammoniacal decomposition, for ammonia consists largely of nitrogen. Every one is familiar with the ammoniacal smell of stables. By manuring the soil we provide our crops with the necessary nitrogen in a usable form.

Let me describe a remarkable series of experiments in Soil Bacteriology. Soil can be sterilized in two ways; first, by heating it, or, secondly, by treating it with chloroform or other similar volatile agents. Plants grown in such sterilized soil, it was found, yielded greatly increased crops, but no one knew why until Russell and Hutchins, of the Rotham-

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stead Experimental Station in England, investigated the matter experimentally. This remarkable field laboratory, as one may call it, was established by Sir John Bennett Lawes in 1843 with an endowment of $500,000, and has done a wonderful amount of good research work in agriculture. Russell and Hutchins found that heat or chloroform, etc., killed many organisms in the soil, but not all. Those that remained increased enormously. For instance, normal soil has seven million bacteria to the gram — a quarter of teaspoonful. After heating, Russell and Hutchins found that there remained alive only four hundred bacteria per gram. But in four days these had increased to six million and later were so much more numerous that they were not even counted. These observers also discovered that in unheated soil there were protozoa — very low forms of animal life — resembling amœbæ, or the white blood cells — which fed on the good bacteria. When these protozoa were killed by heat or chemically, the good bacteria, their enemies being killed, increased enormously and thus enriched the soil by "fixing" the nitrogen of the air. Hence its increased fertility. Manifestly we cannot heat all the soil because eight

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to nine inches of top soil on a single acre weighs about one thousand tons, nor can we chloroform all of our farms. But Hall, the Rothamstead Director, is optimistic and believes that modern science will yet discover a practicable method of fostering the good bacteria in the soil.

But besides these free bacteria in the soil, plants possess a special means of fixing the nitrogen of the air.

From Roman times the farmer has known empirically that peas, beans, etc., and especially clover, greatly improved subsequent crops, but no one knew any reason for this observed fact till modern science discovered it. On the roots of leguminous plants, peas, beans, and the like, are found certain nodules. These nodules are produced by bacteria living in symbiosis with the plant — that is to say, the plant and the bacteria enjoy a common life. (Plate III, Figs. 1 and 2.) These bacteria fix the nitrogen of the air and convert it into compounds which the plant can use. They are Nature's fertilizers. A crop of clover, besides all that which has been utilized in its own yield, leaves a rich legacy of nitrogen behind it in the soil.

The United States Department of Agricul-

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ture now has taken advantage of the above facts and furnishes pure cultures of soil bacteria in liquid form for "inoculating" the soil of our farms.

One method of soil inoculation is by transferring soil rich in bacteria from a prior crop — clover, alfalfa, etc. — to poorer soil, two hundred pounds or more of rich soil over an acre of poor soil. The bacteria of the rich soil multiply enormously and are diffused all through the poor soil.

A slightly different method is provided for farms with no rich soil. A liquid pure culture of the needed bacteria it sprinkled over one hundred to two hundred pounds of the poor soil and thoroughly mixed. This enriched soil is then spread over an acre of poor soil, when the same process of diffusion goes on.

Another and simpler method is to soak the seeds to be planted in a pure culture of the bacteria for a short time in the evening, dry them, and sow them the next morning. But the sun is an enemy of both good and bad bacteria and the treated seed must not be sown in sunny weather. They can be kept for a week or so and still be in good condition, ready to be sown in cloudy weather.

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FIG 1. Nitrogen-fixing Nodules of the Garden Pea

FIG. 2. Nitrogen-fixing Nodules of Alder

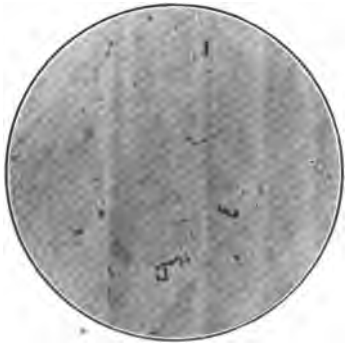

FIG. 3. Fossil Bacteria from Montana

PLATE III

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I am glad to bear my testimony to the admirable work of the Department of Agriculture. We have right here at Brown one of its most useful laboratories in the Bureau of Plant Pathology for investigating the diseases of trees. No other department of our Government is doing better work for Human Welfare.

II. Cancer in Plants

For some years Dr. Erwin F. Smith, of the same Bureau of Plant Pathology, has been conducting some very remarkable experiments on cancer in plants. He believes, and it seems to be a very reasonable probability, that he has discovered the germ which produces cancer in plants — the *Bacillus tumefaciens*. By injecting a little of this germ in solution by a hypodermic syringe at different points in the leaf or stem he apparently can produce at will the various forms of cancer. That one single germ can cause not only cancer proper, but sarcoma and other forms of malignant disease, is a wholly new idea. It must be thoroughly tested by many others before it can be definitely accepted. It seems to be fairly true in plants, but whether true in animals and man is as yet not proved. A visit to his greenhouses in

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Washington, which I enjoyed not long since, was a revelation.

This remarkable discovery, if confirmed by others, will throw a wholly new light on the cancer problem. I have already called attention to the solidarity and similarity of life in humans, animals, and plants. So far we have been unable to discover the cause of cancer in man and animals. This discovery by Dr. Smith, of a mode of producing cancer of all kinds at will in plants by a simple bacterial inoculation, makes one suspect that cancer in man and animals may also be of bacterial origin. It will give a new impetus to the search for such a germ. That it may prove successful will be the devout wish of every lover of his kind.

III. Bacteria in Rocks — Iron Bacteria

It is another very startling fact that bacteria are found not only in the soil, but in rocks and in the ocean. Were the earth and the ocean devoid of bacteria, the world "would soon be uninhabitable to plants and animals." "They were the soil-forming and the soil-nourishing agents of the primal earth" is the striking testimony of Henry Fairfield Osborn. The

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great majority of bacteria are "good bacteria." They assist not only in the fixation of nitrogen, but in breaking up the rocks into fertile soil. In the disintegrating rocks of Alpine summits where no other life existed, Müntz found the rocks swarming with nitrifying bacteria. In 1915 Walcott discovered some fossil bacteria in rocks, the age of which he estimated at 33,000,000 years. (Plate III, Fig. 3.) Such bacteria not only astonish us by their enterprising precocity, but challenge our admiration as the most conspicuous instance of prolonged, modest "watchful waiting" to be discovered on record. The massive limestones of the Tetons are believed to be the product of the algal flora and the calcareous bacteria.

One unusual kind of bacteria are known as "iron bacteria." In sixty-one samples of ferruginous stones from different parts of the world Molisch found bacteria in fifty-seven and suspected their presence in the other four. These bacteria become impregnated with the iron compounds in the water, and, dying, leave the iron as a legacy. In iron springs and bogs the iron thus deposited or secreted is believed to be the source of the so-called "bog iron ore."

But what has all this to do with Medical

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Research? you ask. The reply is self-evident. We owe to these humble, microscopic, living things the origin on the earth of a suitable soil for plants and the fixation of the nitrogen of the air in its various combinations. In the primal world the only nitrogen in existence was the free nitrogen of the air. All the nitrogen compounds in existence and therefore all our vegetable and ultimately our animal foodstuffs have resulted from the ability of the bacteria to fix the free nitrogen of the air.

Had it not been for the researches I have so inadequately described we should not have recognized even the existence of any bacteria. Their great importance is not confined to medicine. Theirs is a world-wide, age-long rôle of supreme importance to the welfare of the entire human race.

What would be our condition to-day if the progress due to Medical Research were suddenly annihilated; if we knew nothing of the bacterial origin of so many diseases, if we were ignorant of the means of preventing them, and were relegated to the atrocities of smallpox, cholera, the black death, and yellow fever? If typhus and typhoid and diphtheria were allowed to run riot as of yore? And who have

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ever been the advance guard in the war against disease? My own profession, I proudly reply. What foes have they not faced — diphtheria, plague, sleeping-sickness, typhus, cholera, yellow fever, all these and more. And scores have made the supreme sacrifice.

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CONCLUSION

What now is the conclusion of the whole matter?

What a serried array of nearly threescore topics I have brought before you in rapid succession! Every disease named has witnessed, during my own professional lifetime, a notable mitigation of its ravages or even its actual or prospective total annihilation.

Yet I have had to omit far more than I have included. Even with these omissions I fear I have wearied you with the long recital.

The warfare of Medical Research on Disease has been most successful. Let me recall only a few of the victories gained: in some, practically complete victories; in others, less complete victories, due largely to neglect of the lessons and maxims of Research: —

Yellow fever	Diphtheria
Typhoid fever	Puerperal fever
Typhus fever	Tuberculosis
Tetanus	Malta fever
Malaria	Anthrax and other diseases of animals

If to these we add the blessings of Anesthesia and the enormous progress in modern

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surgery as a result of Bacteriology and Antisepsis, do you wonder that I glow with enthusiasm at what my profession has done for Humanity during one single lifetime? In these fruitful years Medical Research has done more for Human Welfare than in all the centuries since Time began!

When the Great Peace shall follow the Great War, one conflict will *not* stop. The war of our guild against Disease — as old and as eternal as the war between Ormuzd and Ahriman, between Good and Evil — will never cease until the last disease has been conquered and Humanity has been set free.

In my Jefferson clinic, before I began any operation, my house surgeon always read the history of the case. He recited the name, age, occupation, etc., followed nearly always by this one phrase — "Had the usual diseases of childhood!" At least once a year I interrupted the reading and said to my class, "It is monstrous that childhood should have *any* '*usual* diseases.' Before long I pray God, and you may live to see that joyous day, when our case-histories will read, "Had the usual *health* of childhood."

Research, *Research*, RESEARCH — that is the

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method by which we shall enter into the Paradise of Health, and not for childhood only, but a lifelong Paradise, till Death shall come, not as our last enemy, but as our best friend, to open to us the gates of Immortality.[1]

[1] [Even since these Lectures were delivered new discoveries have been made.

The paraffin treatment of burns has been investigated very actively by many surgeons in Europe and America. The happy result is that our present means of treatment of burns is enormously better than it has ever been before.

Drs. C. G. Bull and Ida W. Pritchett, of the Rockefeller Institute, published in July, 1917, their discovery of the germ of gas gangrene and also of an antitoxin as a remedy. This antitoxin had proved so successful on animals, that later it was used in some of the very rare cases of the same disease in this country and its value to man was confirmed. It is now being tested on a large scale in the war zone in France with the prospect of conquering one of the greatest foes of the wounded soldiers, — a victory comparable only with those over tetanus and typhoid fever.

In addition to this, it is probable that the germ of trench fever has been discovered by Dimond. It is probably a low form of animal life. It is carried, like the plague, by the rat flea. As the trenches are alive with rats its dissemination is easy.

These facts (and there are many other important researches) show how constantly active Medical Research has been in the midst of war, and how all its discoveries have tended to mitigate suffering and conserve human life.]

THE END

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